

Hemodynamic Responses to Hypoxia and Hypercapnia during Acute Normovolemic Hemodilution in Anesthetized Cats

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Abstract: The present study was undertaken to evaluate the effects of hypoxia and hypercapnia on circulatory parameters during acute normovolemic hemodilution. Cats anesthetized with a mixture of α -chloralose and urethane were maintained by positive pressure ventilation. Muscles were paralysed by intramuscular vecuronium (0.1 mg/kg) to eliminate reflex respiratory movements. Cats were exposed to hypoxia (12% O₂ and 7% O₂) and hypercapnia (4% CO₂ and 7% CO₂) at normal hematocrit (Ht $40.1 \pm 2.8\%$) and then at graded levels of normovolemic hemodilution (Ht $24.0 \pm 2.0\%$ and Ht $13.0 \pm 1.5\%$, respectively). Left ventricular pressure (LVP), LV $dP/dt_{\max}$, arterial blood pressure (ABP), heart rate (HR), and right atrial pressure (RAP) were recorded on a polygraph. Cardiac output (CO) was measured using a cardiac output computer. Hemodilution per se did not produce any significant change in ABP, RAP or LV $dP/dt_{\max}$, how-

ever, it produced a significant rise in HR and a significant fall in total peripheral resistance (TPR). Exposure to hypoxic gas mixtures caused significant increases in HR and CO at control Ht; but after hemodilution it caused the reverse effects. Hypercapnia did not produce any significant effect on ABP, LV $dP/dt_{\max}$ or RAP either at control Ht or after hemodilution. Hypercapnia produced a fall in HR, CO and stroke volume (SV) at normal Ht and percent fall in HR response was enhanced following hemodilution. The reversal of chronotropic response to hypoxia and enhanced bradycardia response to hypercapnia, under conditions of acute normovolemic hemodilution would be deleterious as the tissues would become more hypoxic. Such a response may be attributed to altered control mechanisms under such conditions of severe stress. [Japanese Journal of Physiology, 50, 227–234, 2000]

Key words: hemodilution, hypoxia, hypercapnia.

Systemic changes in arterial blood gas evoke many cardio-respiratory responses mediated by central and or peripheral chemoreceptors [1]. Hypoxia causes cardiac depression in patients with acute hypoxemic respiratory failure [2] and depression in myocardial tissue and isolated hearts [3–5]. Hypercapnia decreases myocardial contractility. Gudipati *et al.* [6] and Planta *et al.* [7] have suggested that respiratory acidosis contributes to cardiovascular dysfunction and mortality. Acute respiratory acidosis (pH 7.09, PCO₂ 92 mmHg) decreases left ventricular contractility, increases end systolic volume in anesthetized dogs [8] and causes left ventricle (LV) contractile dysfunction accompa-

nied by an increased oxygen cost of contractility [9]. The fall in myocardial contractility during respiratory acidosis is only partially blocked by the adrenergic activation. Stein and Ellsworth [10] observed that, under the conditions of a severely limited oxygen supply resulting from a combined effect of acute fall in hematocrit and hypoxic ventilation, a diffusion limitation for oxygen resulting from the kinetics of oxygen release from the hemoglobin molecule provides an advantage for oxygen exchange within the capillary network. They suggested that oxygen content rather than PO₂ might be a critical determinant of oxygen supply at low levels of oxygen delivery.

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Acute normovolemic hemodilution is used most often in cardiac surgery but is becoming more popular for a wide variety of non-cardiac procedures [11–13]. It has been suggested that hemodilution is more suitable as a preventive measure rather than as a treatment of micro-circulatory disorders associated with compromised flow [14].

The purpose of the present study was to study the hemodynamic responses to hypoxia and hypercapnia during acute normovolemic anemia. This information would clarify the effects of hypoxia and hypercapnia under the condition of low oxygen carrying capacity of the blood. A previous study by Chapler *et al.* [15] in canine skeletal muscle showed that, with acute normovolemic anemia, there was a significant increase in oxygen uptake. In contrast, Cain [16] observed an increased plasma lactate concentration in the presence of acute anemia in dogs, suggesting a limitation of oxygen supply relative to oxygen demand. In view of these findings, it would be interesting to know the influence of hypoxia or hypercapnia under the preexisting conditions of reduced oxygen carrying capacity of the blood, e.g., acute normovolemic hemodilution.

MATERIALS AND METHODS

Experiments were performed on healthy adult cats ($n=20$) of both sexes, weighing between 3–6 kg. Cats were anesthetized with a mixture of 70 mg/kg α -chloralose (BDH) and 350 mg/kg urethane (E-Merck). One gram α -chloralose was dissolved in 100 ml of distilled water at a temperature between 65 and 70°C. Urethane (5 g) was added to the above solution and the solution was cooled to 37°C before injection. The anesthetic mixture (7 ml/kg) was injected intraperitoneally to the cat. Later, small doses of anesthetic were administered intravenously as required. The level of anesthesia was checked by the state of the pupil. Muscle paralysis was induced with intramuscular vecuronium (0.1 mg/kg) to eliminate reflex respiratory movements.

The trachea was cannulated and cats were ventilated using a respiratory pump (Inco) at the rate of 25/min and with a tidal volume of 12 ml/kg to give a constant ventilation of 300 ml/kg/min. The ventilatory variables were adjusted for normal PO_2 , PCO_2 and pH before starting the cardiovascular measurements. A polyethylene catheter was placed in the descending aorta through a femoral artery for recording arterial blood pressure (ABP) with a pressure transducer (Statham P23 Db). Blood samples were withdrawn anaerobically through this catheter in a heparinised syringe for the measurement of blood PO_2 , PCO_2 and pH

with the help of a blood gas monitor (Radiometer BMS-3MK-2 microsystem and PHM-73 pH electrodes). Hematocrit (Ht) was measured with the help of a microcentrifuge (Janetzki TH 12) and hemoglobin (Hb) was measured using a colorimeter. Once the blood gases of the animals were adjusted in the normal range, by adjusting the ventilatory variables, the ventilation was kept constant throughout the experiment. A right femoral vein was cannulated for intravenous injections and infusion of dextran. A polyethylene catheter was placed in the right atrium through the right external jugular vein for recording right atrial pressure (RAP) with a pressure transducer (Statham model P23 Db). Another polyethylene catheter was placed into the left ventricle (LV) through the left carotid artery for recording left ventricular pressure (LVP) with a pressure transducer (Statham Model P23 Db). The left ventricular pulse was differentiated electronically (differentiator contractility, Lectromed Model 5270) to record LV dP/dt and was used to drive a cardiometer (Lectromed Model 5260) for recording heart rate (HR). All of these variables were recorded on a polygraph (Lectromed, UK). CO was measured by a thermodilution technique using a Swan-Ganz flow directed thermodilution catheter (Model 93-A-131-7F) and a cardiac output computer (COM 1 Edward Co., USA). CO was measured before and after the exchange of blood, and three consecutive readings were taken during each condition. SV was calculated as ml/beat by dividing cardiac output (ml/min) by HR (beats/min). TPR was calculated as mmHg/ml/s.

$$TPR = (MAP - RAP) / CO$$

Cardiovascular measurements were started 30 min after the completion of surgical procedures.

Induction of normovolemic hemodilution.

Normovolemic hemodilution was induced by dextran (molecular weight 150,000) as a substitute for blood. Cats were bled through the femoral arterial catheter and the same volume of dextran was infused through the femoral vein catheter. The dextran (Rallies), a 6% solution of dextran in 5% w/v dextrose, was warmed to 37°C before infusion through the femoral vein catheter. The viscosity of 6% dextran solution is approximately equal to that of plasma. Blood was replaced by dextran in two steps of 30% of total estimated blood volume (5% of the body weight) [17] until Ht fell to 12–14% from 40%. Cardiovascular variables were recorded after a stabilizing period of 30-min following each exchange.

Experimental protocol. All cats ($n=20$) were exposed to the following mixture of gases through a

respiratory pump for 10 min under three conditions (A–C) with a stabilization period of 30 min following each exchange: (A) control, (B) hemodilution 1 (30% blood replacement by dextran), and (C) hemodilution 2 (60% blood replacement by dextran).

(1) Normoxia (room air) (15 min), (2) hypoxia

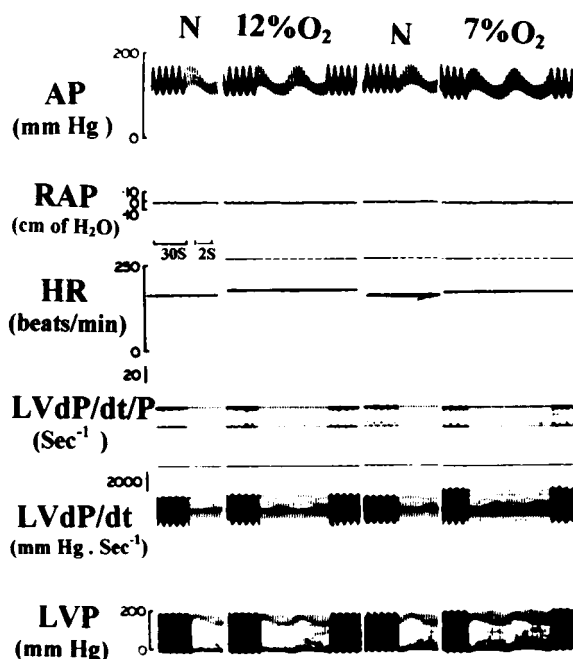


Fig. 1. Representative tracings showing changes in arterial pressure (AP), right atrial pressure (RAP), heart rate (HR), LV dP/dtP , LV dP/dt and left ventricular pressure (LVP) when ventilating cats with normoxic (N) and hypoxic (12% O₂ and 7% O₂) gas mixtures at control Ht ($40.7 \pm 2.8\%$). S, seconds.

(12% O₂) (10 min), (3) normoxia (room air) (15 min), (4) hypoxia (7% O₂) (10 min), (5) normoxia (room air) (15 min), (6) hypercapnia (4% CO₂) (10 min), (7) normoxia (room air) (15 min), (8) hypercapnia (7% CO₂) (10 min).

Blood samples were collected from the femoral arterial catheter at the 10th minute after ventilating the animal with each gas mixture for blood gas analysis. A stabilization/recovery time (normoxic ventilation, 15 min) was given after each respiratory condition. The following hemodynamic variables were recorded: ABP, RAP, LV dP/dt , HR, CO, Ht, Hb, arterial blood gas tension and pH.

Statistical analysis. Data were tabulated for each gas mixture at control Ht, after 1st exchange of blood and after 2nd exchange of blood, and analyzed to provide mean $\pm$ SEM. Two-way ANOVA was used with respiratory conditions and hemodilution as factors. Differences between means were considered to be significant if $p < 0.05$.

RESULTS

Effect of hemodilution

The effects of various gas mixtures on cardiovascular variables are shown in Figs. 1 and 4. On the induction of hemodilution, there was a significant increase in HR and CO and a significant fall in TPR. Mean arterial pressure (MAP) did not show any significant change following the substitution of blood (Tables 2, 5). Hemodilution did not produce any significant effect on LV $dP/dt_{\max}$ (Tables 2, 5) or left ventricular di-

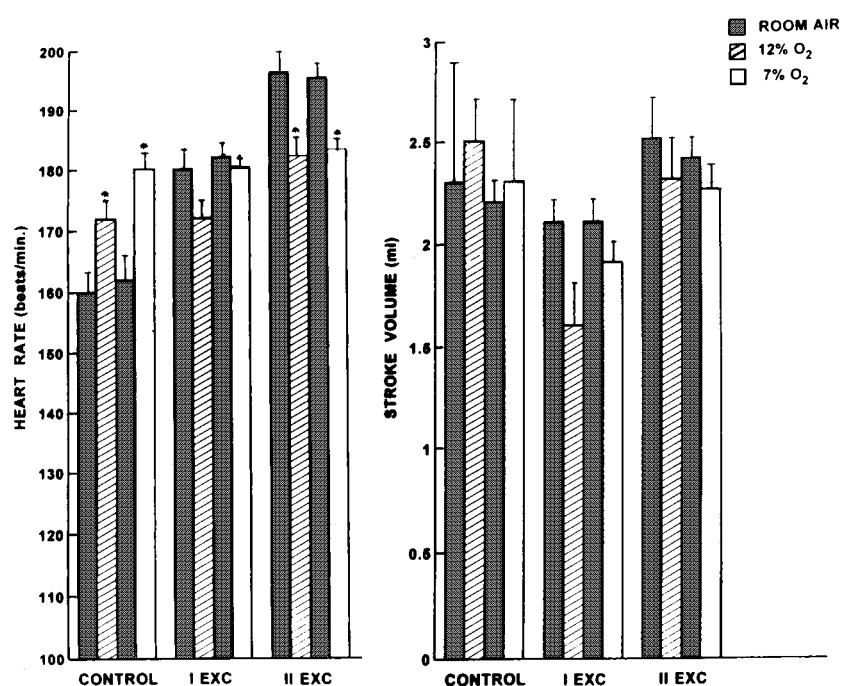


Fig. 2. Effect of hypoxic ventilation (12% O₂ and 7% O₂) on heart rate and stroke volume before (Ht $40.1 \pm 2.8\%$) and after I (Ht $24.0 \pm 2.0\%$) and II (Ht $13.0 \pm 1.5\%$) exchanges of blood with dextran. Each histogram represents means $\pm$ SEM ($n=20$). * $p < 0.05$ significantly different from normoxic ventilation (room air). EXC, exchange of blood with dextran.

astolic pressure (LVDP) (Figs. 1, 4).

Effect of hypoxia

Hypoxia did not produce any significant effect on ABP, LV $dP/dt_{\max}$ or RAP, neither at control Ht nor after the induction of acute hemodilution (Table 2, Fig. 1). Hypoxic gas mixtures (12% O₂ and 7% O₂) produced significant increases in HR and CO at control Ht (Figs. 2, 3). However, after the 1st and 2nd ex-

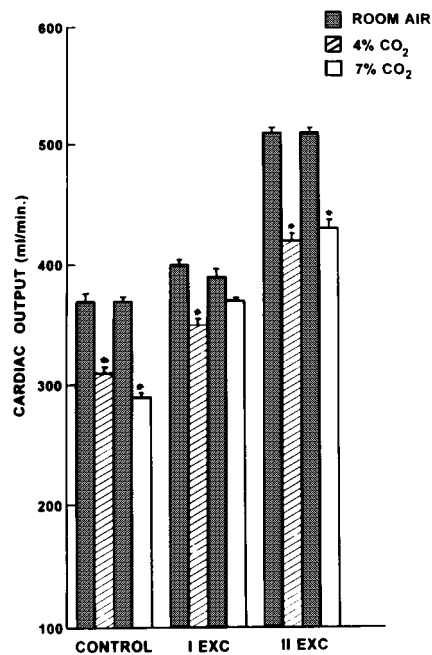


Fig. 3. Effect of hypoxic ventilation (12% O₂ and 7% O₂) on cardiac output before (Ht 40.1±2.8%) and after I (Ht 24.0±2.0%) and II (Ht 13.0±1.5%) exchanges of blood with dextran. Each histogram represents mean±SEM ($n=20$). * $p<0.05$ significantly different from normoxic ventilation (room air). EXC, exchange of blood with dextran.

changes of blood with dextran, ventilation with hypoxic gas mixtures produced decreases in HR, CO and SV (Figs. 2, 3). Arterial blood gas tension and pH changes during hypoxic ventilation before and after the graded exchange of blood with dextran are shown in Table 1.

Effect of hypercapnia

Hypercapnic gas mixtures (4% CO₂ and 7% CO₂) did not produce any significant effect on ABP, LV $dP/dt_{\max}$ or RAP, either at control Ht or after the in-

Table 1. Arterial blood gas tension and pH changes during hypoxic ventilation (12% O₂ and 7% O₂) before and after graded exchanges of blood with dextran.

	PO_2 (mmHg)	PCO_2 (mmHg)	pH
Control			
Normoxia	99±2	33.0±0.82	7.348±0.062
12% O ₂	71±2	30.8±0.7	7.362±0.054
Normoxia	94±2	31.3±0.6	7.353±0.053
7% O ₂	38±2*	28.9±7*	7.401±0.032*
I exchange			
Normoxia	94±2	30.3±0.6	7.401±0.035
12% O ₂	69±1	28.2±0.4	7.417±0.063
Normoxia	92±2	31.2±0.3	7.393±0.034
7% O ₂	41±2*	25.2±0.5*	7.453±0.064
II exchange			
Normoxia	92±2	33.1±0.4	7.397±0.042
12% O ₂	76±2	25.7±0.6	7.424±0.043
Normoxia	92±3	30.9±0.6	7.399±0.028
7% O ₂	43±2*	27.9±0.7*	7.458±0.037*

Values are mean±SEM. * $p<0.05$ compared to normoxic ventilation. PO_2 , partial pressure of oxygen in arterial blood; PCO_2 , partial pressure of carbon dioxide in arterial blood. Normoxia: the animals ventilated with room air.

Table 2. Hemodynamic effects of hypoxic ventilation (12% O₂ and 7% O₂) before and after graded exchange of blood with dextran.

		MAP (mmHg)	LVSP (mmHg)	LV $dP/dt_{\max}$ (mmHg/s)	RAP (mmHg)	TPR (mmHg/ml/s)
Control	Normoxia	127±3	141±2	3,498±42	4.3±0.1	19.4±1.0
(Ht (%): 40.1±2.8)	12% O ₂	129±3	143±2	3,500±45	4.2±0.1	18.9±1.1
(Hb (g/dl): 13.2±1.0)	Normoxia	125±3	140±3	3,502±48	4.3±0.1	19.1±1.0
	7% O ₂	130±2	140±2	3,500±45	4.3±0.1	16.5±1.2
I exchange	Normoxia	127±2	139±2	3,420±50	4.2±0.1	18.8±1.0
(Ht (%): 24.0±2.0)	12% O ₂	127±2	142±3	3,498±48	4.2±0.1	25.5±1.1*
(Hb (g/dl): 9.2±0.8)	Normoxia	126±3	140±2	3,498±50	4.2±0.1	18.7±1.0
	7% O ₂	128±2	140±2	3,500±42	4.2±0.1	21.3±1.2*
II exchange	Normoxia	127±2	139±2	3,498±48	4.2±0.1	15.1±1.0
(Ht (%): 13.0±1.5)	12% O ₂	129±2	138±3	3,300±42	4.2±0.1	17.1±1.1*
(Hb (g/dl): 3.9±1.2)	Normoxia	128±2	138±2	3,428±48	4.2±0.1	15.2±1.0
	7% O ₂	128±2	140±3	3,210±40	4.0±0.1	15.8±1.2

Values are mean±SEM. * $p<0.05$ compared to normoxic ventilation. Ht, hematocrit; Hb, hemoglobin; MAP, mean arterial pressure; LVSP, left ventricular systolic pressure; LV $dP/dt_{\max}$, left ventricular contractility; RAP, right atrial pressure; TPR, total peripheral resistance; Normoxia, normoxic ventilation.

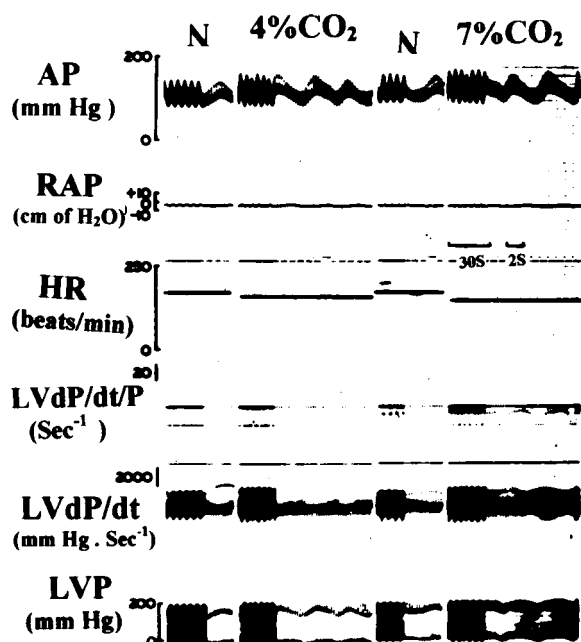


Fig. 4. Representative tracings showing changes in arterial pressure (AP), right atrial pressure (RAP), heart rate (HR), LV $dP/dt/P$, LV dP/dt and left ventricular pressure (LVP) when ventilating cats with normoxic (N) and hypercapnic (4% CO_2 and 7% CO_2) gas mixtures at control Ht ($40.7 \pm 2.8\%$). S, seconds.

Table 3. Percent change in hemodynamic variables during hypoxic ventilation before and after graded exchange of blood with dextran.

	HR (%)	CO (%)	SV (%)
Control			
12% O_2	6.1 ± 1.0	8.1 ± 0.8	9.0 ± 0.2
7% O_2	10.4 ± 1.0	27.7 ± 0.1	9.4 ± 0.6
I exchange			
12% O_2	$-4.4 \pm 1.1^*$	$-25.6 \pm 0.1^*$	$-2.3 \pm 0.4^*$
7% O_2	$-5.4 \pm 0.8^*$	$-10.2 \pm 0.8^*$	$-9.5 \pm 0.2^*$
II exchange			
12% O_2	$-6.6 \pm 0.2^*$	$-16.1 \pm 0.2^*$	$-8.0 \pm 0.8^*$
7% O_2	$-5.6 \pm 0.8^*$	$-4.2 \pm 0.8^*$	$-8.3 \pm 0.2^*$

Values are mean $\pm$ SEM. * $p < 0.05$ significantly different response to hypoxia from corresponding value before exchange of blood. HR, heart rate; CO, cardiac output; SV, stroke volume.

duction of acute normovolemic hemodilution (Table 5, Fig. 4). Hypercapnia produced a fall in HR, CO and SV (Figs. 5 and 6). However, percent fall in HR was increased ($p < 0.05$) after the 1st and 2nd exchanges of blood with dextran (Fig. 5, Table 6). Arterial blood gas tension and pH changes during hypercapnic ventilation are shown in Table 4.

Table 4. Arterial blood gas tension and pH changes during hypercapnic ventilation (4% CO_2 and 7% CO_2) before and after graded exchange of blood with dextran.

	PO_2 (mmHg)	PCO_2 (mmHg)	pH
Control			
Normoxia	90 ± 2	30.5 ± 0.6	7.390 ± 0.036
4% CO_2	107 ± 3	$40.5 \pm 0.5^*$	$7.262 \pm 0.062^*$
Normoxia	92 ± 2	31.1 ± 0.2	7.355 ± 0.028
7% CO_2	102 ± 3	$45.8 \pm 0.3^*$	$7.220 \pm 0.062^*$
I exchange			
Normoxia	98 ± 2	29.7 ± 0.4	7.366 ± 0.032
4% CO_2	100 ± 2	$32.9 \pm 0.5^*$	$7.353 \pm 0.041^*$
Normoxia	99 ± 2	30.0 ± 0.6	7.366 ± 0.038
7% CO_2	116 ± 3	$46.4 \pm 0.4^*$	$7.246 \pm 0.062^*$
II exchange			
Normoxia	92 ± 2	30.9 ± 0.4	7.384 ± 0.054
4% CO_2	101 ± 3	39.8 ± 0.3	$7.272 \pm 0.053^*$
Normoxia	99 ± 2	30.2 ± 0.2	7.397 ± 0.051
7% CO_2	111 ± 2	$44.4 \pm 0.6^*$	$7.224 \pm 0.043^*$

Values are mean $\pm$ SEM. * $p < 0.05$ compared to normoxic ventilation. PO_2 , partial pressure of oxygen in arterial blood; PCO_2 , partial pressure of carbon dioxide in arterial blood. Normoxia: the animals ventilated with room air.

DISCUSSION

The present study evaluated the cardiovascular effects of hypoxia (12% O_2 and 7% O_2) and hypercapnia (4% CO_2 and 7% CO_2) during acute hemodilution. The results demonstrated that both hypoxic gas mixtures at control Ht produced a significant rise in HR and CO with no significant changes in ABP or LV dP/dt_{max} . However, after the induction of acute normovolemic hemodilution, the responses to similar concentrations of hypoxic gas mixtures were directionally opposite to those recorded at control Ht. Hypoxic gas mixtures produced decreases in HR and CO in cats subjected to acute hemodilution. During hypoxic ventilation, the sympathetic response to hypoxia depends on the interactions between chemoreceptor stimulation and associated hyperventilation. The sympathetic response to chemoreceptor stimulation may represent the net effect of the excitatory influence of chemoreflexes and inhibitory influence of pulmonary afferents and cardio pulmonary afferents [18]. However, in the present study, the animals were artificially ventilated, which eliminated the influence of hyperventilation and any change in the input due to pulmonary afferent will not contribute to change in sympathetic activity during chemoreceptor stimulation by hypoxia. The increase in HR during acute hemodilution is mediated mainly through vagi [19], however, mechanisms other than the vagal and adrenergic system are also capable of

Table 5. Hemodynamic effects of hypercapnic ventilation (4% CO₂ and 7% CO₂) before and after graded exchange of blood with dextran.

		MAP (mmHg)	LVSP (mmHg)	LV dP/dt _{max} (mmHg/s)	RAP (mmHg)	TPR (mmHg/ml/s)
Control (Ht (%): 40.1±2.8) (Hb (g/dl): 13.2±1.0)	Normoxia	124±3	140±2	3,428±52	4.3±0.1	19.0±1.0
	4% CO ₂	124±3	138±2	3,400±50	4.0±0.1	23.5±1.1*
	Normoxia	125±3	140±3	3,128±50	4.3±0.1	19.1±1.0
	7% CO ₂	124±3	140±2	3,398±45	4.2±0.1	24.9±1.2*
I exchange (Ht (%): 24.0±2.0) (Hb (g/dl): 9.2±0.8)	Normoxia	126±3	140±2	3,450±48	4.0±0.1	18.6±1.0
	4% CO ₂	127±3	140±3	3,398±42	4.2±0.1	21.9±1.1*
	Normoxia	127±3	140±2	3,050±50	4.2±0.1	18.8±1.0
	7% CO ₂	126±3	139±2	3,400±45	4.0±0.1	21.0±1.2*
II exchange (Ht (%): 13.0±1.5) (Hb (g/dl): 3.9±1.2)	Normoxia	128±2	138±2	3,428±48	4.2±0.1	15.2±1.0
	4% CO ₂	126±2	138±2	3,300±42	4.2±0.1	17.9±1.1*
	Normoxia	126±2	138±2	3,400±50	4.2±0.1	15.0±1.0
	7% CO ₂	125±3	136±2	3,420±50	4.2±0.1	17.5±1.2*

Values are mean±SEM. * $p<0.05$ compared to normoxic ventilation. Ht, hematocrit; Hb, hemoglobin; MAP, mean arterial pressure; LVSP, left ventricular systolic pressure; LV dP/dt_{max}, left ventricular contractility; RAP, right atrial pressure; TPR, total peripheral resistance; Normoxia, normoxic ventilation.

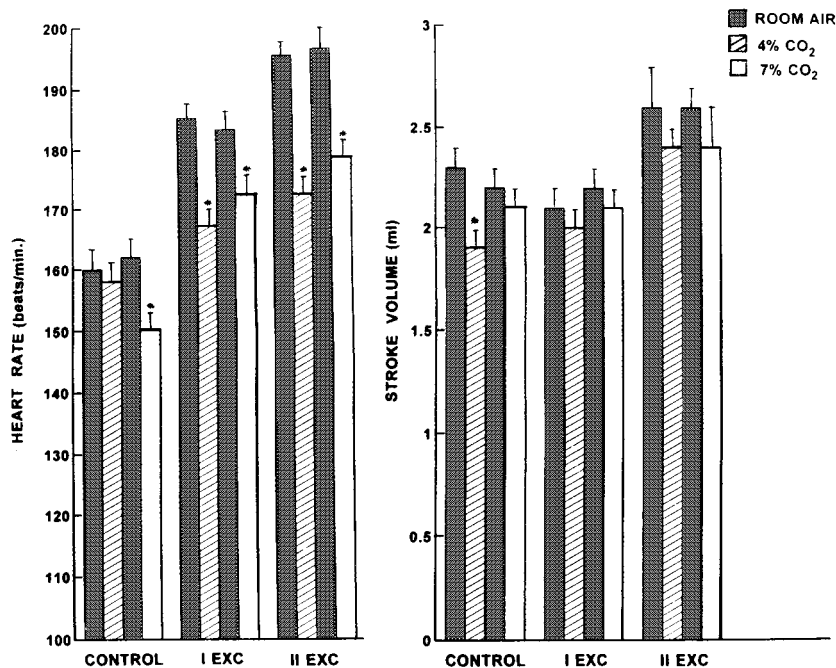


Fig. 5. Effect of hypercapnic ventilation (4% CO₂ and 7% CO₂) on heart rate and stroke volume before (Ht 40.1±2.8%) and after I (Ht 24.0±2.0%) and II (Ht 13.0±1.5%) exchanges of blood with dextran. Each histogram represents mean±SEM ($n=20$). * $p<0.05$ significantly different from normoxic ventilation (room air). EXC, exchange of blood with dextran.

regulating CO under conditions of stress [20, 21]. In the present study, the tachycardia response to hypoxia during acute hemodilution was reversed, whereas earlier studies in unanesthetized animals have shown maintained or increased CO, HR, ABP and LV dP/dt_{max} in response to hypoxia [22, 23]. The altered response to hypoxia under the conditions of acute hemodilution probably indicates an autonomic imbalance under such conditions of severe stress. Changes in HR and ABP produced by chemical stimuli are thus the net result of these complicated interactions and differ greatly in different experimental conditions in various animal species [24]. Responses also differ at

different levels of chemical stimuli and condition of anesthesia [25]. However, in the present study, the anesthetic used was the same in both groups, and blood gas tension and pH changes due to hypoxia were also not significantly different in between the groups.

Hypercapnic gas mixtures did not produce any significant effect on ABP or LV dP/dt_{max}, which is in agreement with earlier studies demonstrating that respiratory acidosis is not depressant to the heart except at a very high level of PCO_2 [26, 27]. It has been demonstrated that the compensatory mechanisms are operative on exposure to hypercapnia in intact animal

Table 6. Percent change in hemodynamic variables during hypercapnic ventilation before and after graded exchange of blood with dextran.

	HR (%)	CO (%)	SV (%)
Control			
4% CO ₂	-1.2±0.1	-16.2±0.2	17.3±0.2
7% CO ₂	-7.4±0.8	-21.6±0.6	-13.6±0.6
I exchange			
4% CO ₂	-9.7±1.0*	-12.5±0.7	-9.0±0.2
7% CO ₂	-6.0±0.9	-5.1±0.8	-8.6±0.4
II exchange			
4% CO ₂	-11.7±0.1*	-17.6±0.6	-7.6±0.6
7% CO ₂	-9.1±0.2*	-15.6±0.7	-7.6±0.7

Values are mean±SEM. * $p < 0.05$, significantly different response to hypercapnia from corresponding value before exchange of blood. HR, heart rate; CO, cardiac output; SV, stroke volume.

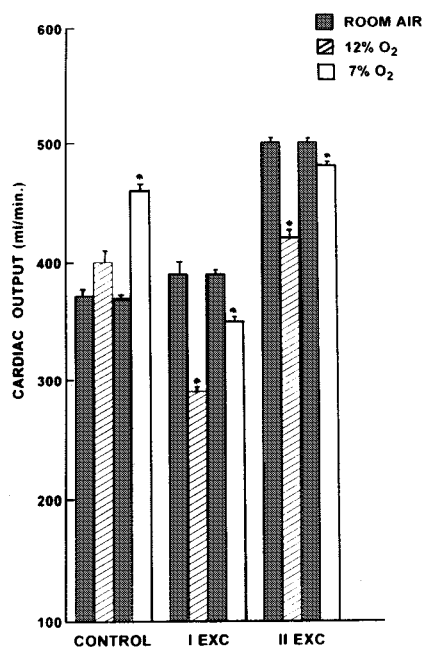


Fig. 6. Effect of hypercapnic ventilation (4% CO₂ and 7% CO₂) on cardiac output before (Ht 40.1±2.8%) and after I (Ht 24.0±2.0%) and II (Ht 13.0±1.5%) exchanges of blood with dextran. Each histogram represents mean±SEM ($n=20$). * $p < 0.05$ significantly different from normoxic ventilation (room air). EXC, exchange of blood with dextran.

preparations [28, 29]. In the present study, ABP and LV dP/dt_{max} were unaltered during hemodiluted conditions, indicating maintained adrenergic reflexes under such conditions. Heart rate responses to acidosis are known to depend on the basal HR and anesthetic agent [30]. Respiratory acidosis decreases HR if the basal HR is high and increases the HR if the basal HR is low. However, the chronotropic effect of respiratory acidosis involves both peripheral and central receptors

acting through vagal efferents [30]. If similar mechanisms are operative during the hemodiluted condition, higher basal HR could probably be responsible for the bradycardia response to hypercapnia. The altered responses to hypoxia and hypercapnia during acute normovolemic hemodilution observed in the present study may call anesthesiologist's attention to clinical practice of hemodilution.

CONCLUSION

In conclusion, we have shown that acute normovolemic hemodilution reversed tachycardia response to hypoxia, possibly due to either initial higher HR in hemodiluted conditions or to an autonomic imbalance under severe conditions of hypoxia and hemodilution. Hypercapnia produced bradycardia during both control and hemodiluted conditions. However, in the hemodiluted condition, bradycardia response was enhanced. The possible reason for the bradycardia could be a higher basal HR after hemodilution.

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