Medical Journal of the
Islamic Republic of Iran

Volume 9
Number 4
Winter 1374
February 1996

CARDIOVASCULAR RESPONSES TO HYPERCAPNIA AND VARYING LEVELS OF ARTERIAL pH IN THE ANESTHETIZED CAT

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ABSTRACT

Effects of acute hypercapnia on the cardiovascular system (CVS) were studied in the anesthetized cat. After surgery the animal was exposed to a gas mixture of 12% CO_2 and 25% O_2 in nitrogen, and hypercapnia with low levels of arterial pH (pHa) was produced for 20 minutes. In the second run the same level of hypercapnia was induced by ventilating the same cat from the above gas mixture but pHa was kept normal by a slow and continuous infusion of THAM (0.5 mM/kg/min). Results of this study showed that hypercapnia increased aortic flow and induced peripheral vasodilation. Hypercapnia produced tachycardia in the presence of arterial acidosis whereas in its absence this response reversed to bradycardia. Hypercapnia increased mean arterial blood pressure (Pa) by 20% during low pHa, whereas this increase was only 10% in the absence of arterial acidosis. Therefore, it is concluded that hypercapnia in conjunction with arterial acidosis has a much stronger stimulatory influence on the CVS via different arterial chemoreceptors.

Keywords: Hypercapnia; acidosis; cardiovascular system; arterial chemoreceptors.
MJIRI, Vol. 9, No. 4, 341-345, 1996.

INTRODUCTION

Hypercapnia is the elevation of arterial CO_2 tension which, in acute conditions, is usually accompanied with low arterial blood pH. Hypercapnia is shown to induce arteriolar vasodilation and elevation of cardiac performance.[1,4] Despite voluminous literature devoted to the influences of hypercapnia on the CVS, results are contradictory and confusing.[1,4,11] It has been shown that hypercapnia in the cat increases the sensitivity of carotid bodies (cb) to hypoxia, but this only has a transient effect on aortic bodies (ab).[5] Arterial acidosis, on the other hand, stimulates ab more strongly.[9] Direct stimulation of these chemoreceptors has been shown to have an intense influence on the CVS.[7,13] Although the influence of combined hypoxia and varying levels of hypercapnia on the CVS and endocrine secretion have been studied in the dog,[1,4,10] the CVS responses to acute hypercapnia during normoxia in the presence or absence of arterial acidosis have as yet not been evaluated.

So far, the arterial chemoreceptor neural responses to hypoxia, hypercapnia and acidosis have been studied in the cat,[5,9] but there is no information concerning the CVS responses of this animal to hypercapnia. Since our knowledge about the influences of hypercapnia and acidosis on neural activity of arterial chemoreceptors are obtained from experiments performed in the cat, we continued our research in the cat and tried to study the influences of hypercapnia and acidosis on the CVS.

Table I. Arterial blood pH, $PaCO_2$ and PaO_2 during hypercapnia with arterial acidosis and recovery.+

Time condition	pHa	$PaCO_2$ mmHg	PaO_2 mmHg
Control	7.337 ± 0.002	35.0 ± 0.9	120 ± 8
Expt min 3	7.116 ± 0.010*	55.0 ± 2.4*	120 ± 9
Expt min 10	7.047 ± 0.010*	63.0 ± 2.4*	116 ± 6
Expt min 20	7.040 ± 0.010*	64.0 ± 2.4*	115 ± 6
Recv min 3	7.240 ± 0.020*	38.0 ± 2.1*	114 ± 9
Recv min 10	7.316 ± 0.010	35.0 ± 2.1	115 ± 8
Recv min 20	7.323 ± 0.010	36.0 ± 1.8	120 ± 9

Expt = experiment; Recv = recovery.

+ Values are expressed as mean ± SE.

* Significantly different from that of normal cats at $P \leq 0.05$.

Results of this study would hopefully clear the controversies that exist between the reported influences of hypercapnia on the CVS and the role of arterial chemoreceptors in regulating this system.

MATERIALS AND METHODS

Experiments were carried out on cats anesthetized with 30 mg/kg intraperitoneal injections of sodium pentobarbital as a routine procedure.[3,5,6] The right femoral vein was cannulated in order to infuse dextrose saline, tris hydroxymethyl amino methane (THAM) and the anesthetic agent. The right femoral artery was cannulated in order to measure arterial blood pressure and for intermittent collections of blood samples. Tracheostomy was done for artificial ventilation. Arterial PO_2, PCO_2 (PaO_2, $PaCO_2$) and pHa were measured with a micro blood gas analyzer (Radiometer pH M 72 Mk2). A left lateral thoracotomy was performed at the fifth interspace and the pericardium was cut to expose the heart. The ascending aorta was dissected carefully from the pulmonary artery. An electromagnetic probe (No. 5) was placed about the root of the aorta. A third cannula was placed into the right atrium in order to measure its pressure. The heart rate was counted from arterial pressure traces. A thermistor probe was placed rectally to measure and maintain the core temperature at 37±1°C by using a heating plate. At the end of surgery the animal was left to rest for three hours in order to eliminate the effects of surgical stress on the CVS as much as possible.

Experimental procedure

Experiments were performed on 22 cats. Three hours after surgery hypercapnia with a low arterial pH (hypercapneic acidosis; H-A) was induced for 20 minutes by artificially ventilating the cat from a gas

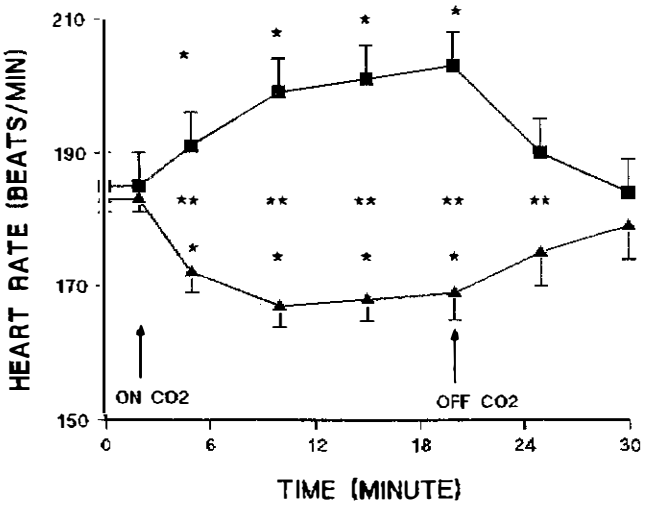

Fig. 1. Heart rate during H-A (■) and H-N (▲). (★ = significantly different from control. ★★ = significantly different from each other, $P < 0.05$).

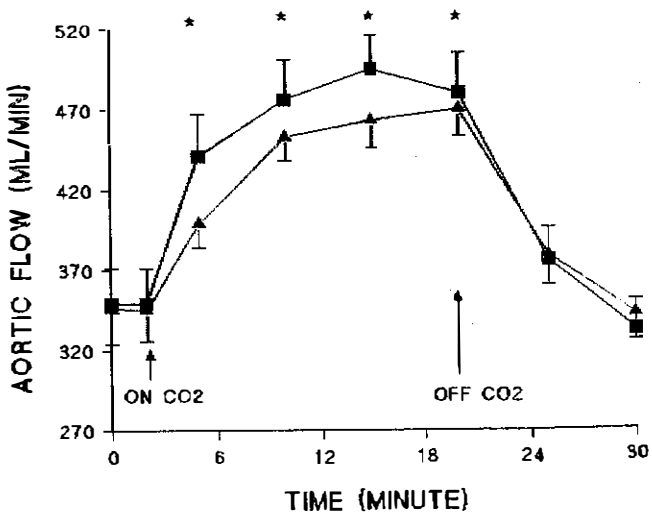

Fig. 2. Aortic flow during H-A (■) and H-N (▲) . (★ = significantly different from control, $P < 0.05$)

mixture containing 12-15% CO_2 and 25% O_2 in N_2. The animal was then switched to room air and CV parameters recorded for another 10 minutes and the results considered as recovery (recv). An hour later the buffering capacity of the blood was increased by a slow intravenous infusion of a one molar solution of THAM in normal saline (0.5 ml/kg/min).[12] The animal was then exposed to the same gas mixture and the same level of hypercapnia was induced. Here the reduction of blood pH was minimal, hence this condition is considered as hypercapnia with normal arterial pH (H-N; Table II). Respiratory rates, tidal volume and other parameters were kept constant in order to lower the interaction of lung stretch receptors with the direct and reflex effects of hypercapnia on the CVS as much as possible.[3]

All recordings were made on an 8 channel Grass

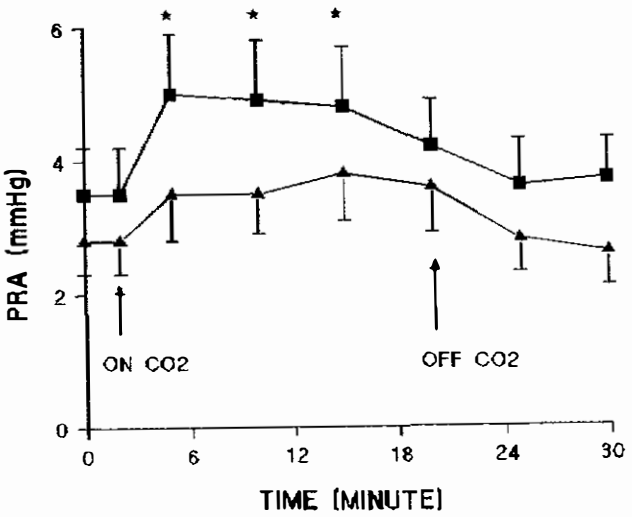

Fig. 3. Right atrial pressure during H-A (■) and H-N (▲).

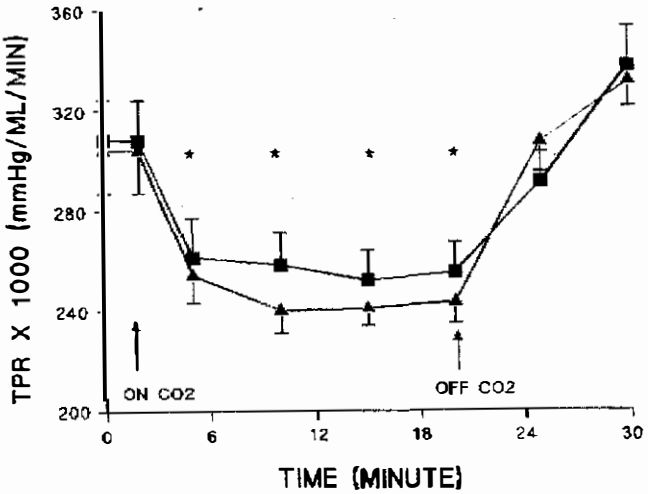

Fig. 4. Total peripheral resistance during H-A (■) and H-N (▲).

polygraph. Mean arterial blood pressure (Pa) and mean right atrial pressure (PRA) were recorded continuously by damping pressure traces electronically. Mean and pulsatile aortic flow were recorded by connecting the flow probe to a Carolina flow meter attached to the polygraph. In recording the mean aortic flow (Qa), zero flow was taken to the portion of the record preceding the sharp systolic upstroke. Total peripheral resistance (TPR), excluding coronary resistance, was calculated by dividing Pa minus PRA in mmHg by aortic flow in ml/min.

Statistical analysis

All results were expressed as means and standard error of the mean. The data were analyzed using analysis of variance. Duncan's new multiple range test was used to find statistical differences between the means when the probability value was equal to or less than 0.05 ($P \leq 0.05$).

Table II. Arterial blood gases during hypercapnia with normal pH.+

Time	pHa	$PaCO_2$ mmHg	PaO_2 mmHg
Control	7.412 ± 0.02	31.8 ± 1.3	120 ± 8
Expt min 3	7.313 ± 0.02	55.2 ± 1.16*	120 ± 9
Expt min 10	7.286 ± 0.09	60.1 ± 1.6*	115 ± 9
Expt min 20	7.268 ± 0.08	68.1 ± 3.6*	116 ± 6
Recv min 3	7.381 ± 0.01	48.0 ± 3.1*	114 ± 9
Recv min 10	7.422 ± 0.02	38.0 ± 3.1	115 ± 9
Recv min 20	7.446 ± 0.01	38.3 ± 2.5	120 ± 9

+ Values are expressed as mean ± SE.

* Values are significantly different from control at $P \leq 0.05$.

RESULTS

Tables I and II show blood pH and gas values during the experiment. In H-A the increased $PaCO_2$ was accompanied by a concomitant reduction in pHa, but in H-N the changes in pHa were statistically insignificant.

Cardiac performance

Fig. 1 shows that heart rate (HR) decreased significantly during H-N whereas this response was reversed to tachycardia during H-A. Fig. 2 represents that there were significant and similar increments in Qa in both conditions. Full recovery occurred 10 minutes after cessation of hypercapnia.

Right atrial pressure (PRA)

Fig. 3 shows that there was a significant increase in PRA only during the first 10 minutes of H-A.

Arterial vascular tone and blood pressure

Fig. 4 shows that there is a 20% reduction in the values of TPR during hypercapnia. As shown in Fig. 5, there was a slight decrease in the values of Pa during the first two minutes of H-N which later on reversed to a significant rise. Whereas during H-A, Pa increased right away, after stabilization these increments were 10% and 20%, respectively. These changes returned back to control values after switching the cat to room air.

DISCUSSION

Many studies have evaluated the effects of hypercapnia on the CVS, but almost none have differentiated the responses of this system to hypercapnia without the influence of arterial acidosis. Earlier reports have shown that a concomitant elevation of $PaCO_2$ and acidosis would affect CVS activity in the

dog, but these reports are debatable.[1,3,6,12] In this study we first tried to see if there would be any differences between the effects of hypercapnia on the CVS of the cat from that of the dog. Then we tried to find out whether controlling the pH of arterial blood would alter these responses to hypercapnia. Respiratory rate and tidal volume were kept constant during the experiment to diminish the interaction of lung stretch reflexes with that of arterial chemoreceptors, as proved to be the case.[9]

Acute hypercapnia lowers intercellular and cerebrospinal fluid pH independent of arterial blood pH,[3] and activates sympathetic gastric nerves via central chemoreceptors independent of arterial chemoreceptors.[14] Therefore, in this study the local effects of hypercapnia on pacemaker cells, myocardium, vascular beds and hopefully the central nervous system remained constant in both conditions to eliminate their interactions with chemoreceptor reflexes as much as possible. The results of this study would give us a new insight concerning the influences of hypercapnia alone and in conjunction with acidosis on the CVS of the cat.

The local influences of hypercapnia and acidosis are shown to be vasodilation and cardiac depression.[7,11] On the other hand, arterial chemoreceptors (ab and cb) which directly sense H ion concentrations and arterial blood gases are shown to have different sensitivities to $PaCO_2$ and pHa,[2,5,9] and their separate or combined stimulation have various influences of the CVS.[6,7,11,13] It is interesting to note that the cardiac system showed a complicated response to both types of hypercapnia. There was an increase in cardiac output (Fig. 2), and although heart rate increased during H-A, this response was completely opposite during H-N (Fig. 1). These results made us believe that not only are CVS responses of the cat to hypercapnia different from that of the dog but also that the presence or absence of acidosis makes the whole story different.

The increased cardiac output might be the outcome of augmented myocardial contractility and venous return,[5] because the negative chronotropic effects of hypercapnia during H-N could not alter this elevation. In isolated preparations, lactic acidosis has been shown to have negative inotropic and chronotropic effects on the heart,[12] whereas stimulation of arterial chemoreceptors have opposite effects through sympathetic stimulation and increased adrenal secretion of epinephrine.[6,11] Hypercapnia independent of arterial acidosis lowers the intracellular pH of myocardial cells.[1,14] Therefore, the level of intracellular pH was (hopefully) identical in both conditions. If this is the case the decreased heart rate observed during H-N could be attributed to intracellular acidosis as concluded by Rothe et al,[11] and a weaker stimulatory response of arterial chemoreceptors

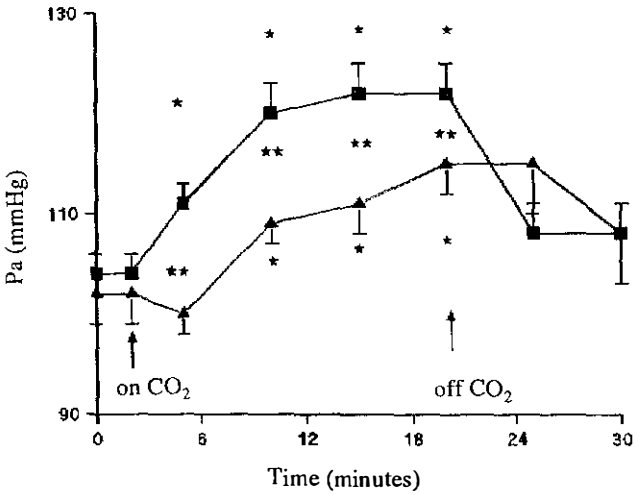

Fig. 5. Mean arterial pressure during H-A (■) and H-N (▲) (★★ = significantly different from each other, $P < 0.05$).

to hypercapnia in the absence of acidosis. Hence in the presence of acidosis, hypercapnia could overcome the depressing effects of intracellular acidosis due to stronger stimulation of cb chemoreceptors.[6,9]

Venous return is another factor which directly influences cardiac output. PRA is a good indicator of the increment of venous return when there is a concomitant increment in cardiac output in the normal functioning heart. Although in this study we could not directly measure myocardial contractility, from the results of other investigators we can say that there was an increase in cardiac performance mainly in response to stimulation of arterial chemoreceptors.[6,13] Furthermore, Rothe et al. showed that hypercapnia increased capacitance vessel tone through arterial chemoreceptor stimulation.[11] Therefore, the significant elevation of PRA observed during H-A accompanying the increased cardiac output is a good sign of the increment of venous return (Fig. 3).

TPR in conjuction with the measurement of arterial blood pressure clearly obviated the responses of the arterial system to H-A and H-N. There was a significant reduction in TPR in both conditions (Fig. 4) which is in agreement with the results of Rothe et al.[11] It has been shown that H-A produces moderate arteriolar vasodilation in the dog.[1] Despite our expectation that TPR would decrease much more during hypercapnia in the presence of arterial acidosis, we found that changes were similar in both conditions (Fig. 4). Pokorski et al. have shown that metabolic acidosis mainly stimulates ab.[9] Although stimulation of ab by arterial acidosis might have increased sympatho-adrenal activity much more during H-A, it seems that it was not able to diminish the direct local vasodilatory effects of acidosis as reported by others.[10,11,13]

Elevation of cardiac output in the presence of arterial vasodilation in this study is the main cause of increased Pa (Fig. 5). Earlier reports have reiterated that combined stimulation of both ab and cb would overcome the direct vasodilatory influences of systemic hypoxia in the cat.[6] Although arterial vessels had a vasodilatory response to hypercapnia (Fig. 4), we still think that combined stimulations of ab and cb were the main cause of a much greater increase in Pa during H-A. The lower activity of ab during H-N made the elevation of Pa less pronounced than what was observed during H-A (Fig. 5).

In summary, the results of this study indicated that a combination of arterial acidosis and hypercapnia has a greater and more forceful stimulatory influence on arterial chemoreceptors. This stimulation eliminates the direct depressing effects of hypercapnia and acidosis on arterial blood pressure, cardiac performance and heart rate.

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