Volume 14
Number 1
Spring 1379
May 2000

THE EFFECT OF ARTERIAL O_2 SATURATION AND HEART RATE ON BLOOD PRESSURE DURING HYPOXIA

M.H. BOSKABADY, S. KARBANDI, AND A. ABEDINZADEH

From the Dept. of Physiology, Ghaem Medical Center, Mashhad University of Medical Sciences, Mashhad, I.R. Iran.

ABSTRACT

A periodic increase in blood pressure (BP) occurs during apneic episodes in patients with obstructive sleep apnea (OSA). Several factors including hypoxemia and an increase in heart rate (HR) were reported to be responsible for this increased BP.

To examine the contribution of these two factors in increasing BP, 35 healthy male subjects (mean age ±SD= 23.64 ±3.80) were studied in three experimental conditions, each condition for two minutes, including; breathing room air at rest (normoxic), breathing low O_2 (10%) air (hypoxic), and exercising on an ergometer while breathing room air (exercise). During the last minutes of each condition, changes in mean BP ($\triangle$mBP), HR ($\triangle$HR), and arterial O_2 saturation ($\triangle SaO_2$) were measured.

The results showed that $\triangle$mBP and $\triangle$HR were significantly higher in both hypoxic and exercise conditions than normoxic condition ($p<0.001$ for both cases). However, $\triangle SaO_2$ was significantly lower in the hypoxic state compared to normoxic conditions. There was no significant difference in $\triangle$HR between hypoxic and exercise groups, but both $\triangle$mBP and $\triangle SaO_2$ were significantly lower in hypoxic than exercise conditions ($p<0.005$ and $p<0.001$ for $\triangle$mBP and $\triangle SaO_2$, respectively). There was a weak correlation between $\triangle$mBP and $\triangle$HR in the hypoxic condition ($r=0.3$, $p<0.05$), but the correlation between $\triangle$mBP and $\triangle$HR in the exercise condition was stronger ($r=0.57$, $p<0.001$).

These results indicated that although hypoxemia contributes to increased BP during hypoxia, an increase in HR is a stronger mechanism for this phenomenon.

MJIRI, Vol. 14, No. 1, 37-41, 2000

Keywords: Blood pressure, Heart rate, O_2 Saturation, Hypoxia.

INTRODUCTION

Acute and chronic elevations of blood pressure (BP) are documented in obstructive sleep apnea (OSA), and in some cases chronic hypertension has been reversed by treatment of apnea.[1] These post-apneic blood pressure elevations account for nocturnal hypertension in patients with OSA[2] and may contribute to an excess of morbid cardiovascular events during sleep.[3]

Several mechanisms including arterial hypoxemia,[4,5] intrathoracic pressure changes,[6] carbon dioxide retention and acidosis,[7] disruption of sleep architecture,[8] and alteration of salt fluid balance[9] have been reported to cause this increased blood pressure.

Among these factors arterial hypoxemia has received more attention. Elevation of systolic blood pressure during apnea has been correlated to the degree of oxygen desaturation,[10] and oxygen administration is reported to

Correspondence: M.H. Boskabady, M.D., Ph.D., Dept. of Physiology, Ghaem Medical Center, Mashhad, Zip Code 91735, I.R. Iran.

reduce the acute elevation of blood pressure during apnea.[11] Hypoxia is known to increase postganglionic sympathetic activity[12] and combined hypoxia and hypercapnia (as seen in apnea) synergistically increase sympathetic nerve response.[13] However HR usually manifests a similar periodic behaviour, with dramatic increases in both BP and HR at about the resumption of respiration after each apnea.[14]

Therefore, in the present study, the contribution of hypoxia and increased HR by breathing low oxygen air on one occasion and exercising on an ergometer while breathing room air on another occasion on blood pressure were examined in normal subjects.

MATERIALS AND METHODS

Subjects

Thirty-five male subjects with ages between 19 and 37 years (mean ±SD= 23.64 ±3.80), body weight ranging from 52.3 to 98.7 kg (mean ±SD= 67.98 ±10.87), and height between 152and 187 cm (mean ±SD= 172.34 ±8.02) served as subjects in this study. All subjects were non-smokers and had no history or symptoms of cardiovascular or respiratory disease (excluding the common cold) that required treatment. All experiments were carried out in the mid morning. The protocol was approved by the Ethical Committee of our institution and each subject gave informed consent.

Protocols

The experiments of this study were made on each subject in four different conditions at 15 minute intervals and in random order. In three of the conditions (experimental conditions), subjects breathed through a mouthpiece connected to a three-way tube. Inspiratory and expiratory airflows were separated by two "one way" valves and expiratory air was conducted through a small spirometer (Haloscale Wright Respirometer HS 23428, Ferraris Medical Limited, England). In one of these conditions, subjects breathed room air for 2 minutes (normoxic condition). On another occasion they breathed through a large Douglas bag containing 10% O_2 and 90% N_2 until SaO_2 reached 85%, and continued for another 2 minutes (hypoxic condition). In the third condition subjects breathed room air while exercising on an ergometer (Model 405 Tunturi, Finland) until the heart beat reached the same value as that obtained during hypoxic condition and continued for another 2 minutes (exercise condition). In another condition subjects breathed room air without a mouth piece (rest condition).

Measurement

During the last minutes of the experiments in each condition the following parameters were measured; arterial oxygen saturation (SaO_2) and heart rate using a pulse oximeter (Model 504/504P, Criticare System Inc., USA), systolic, diastolic, and mean blood pressure using an automatic

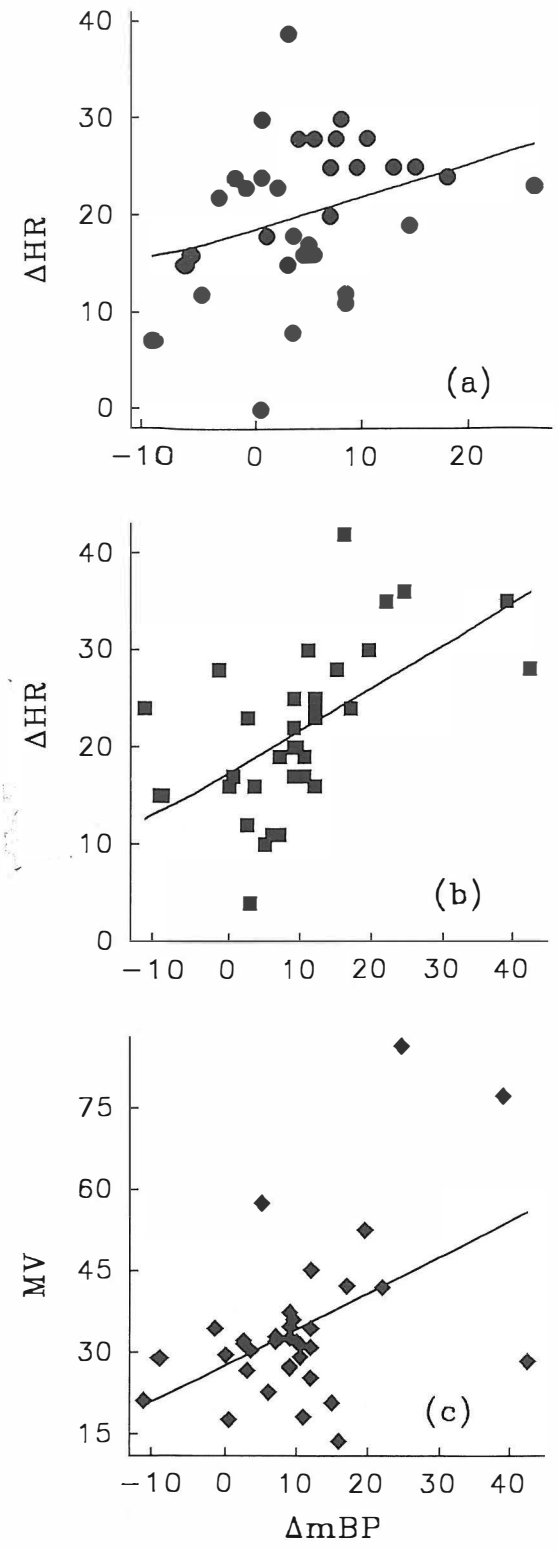

Fig. 1. (a) Correlation between △mBP and △HR in hypoxic condition: r=0.30, $p<0.05$. (b) Correlation between △mBP and △HR in exercise condition: r=0.57, $p<0.001$. (c) Correlation between △mBP and MV in exercise condition: r=0.47, $p<0.005$. (n=35 for all three cases)

Table I. Values of minute ventilation (MV) and changes in arterial oxygen saturation ($\triangle SaO_2$), heart rate ($\triangle HR$), mean blood pressure ($\triangle mBp$), systolic blood pressure ($\triangle sBP$), and diastolic blood pressure ($\triangle dBP$) during normoxia, hypoxia and exercise compared to those of resting conditions.

Parameter	Normoxia	Hypoxia	St. Dif. *vs* N	Exercise	St. Dif. *vs* N	St. Dif. *vs* H
$\triangle SaO_2$	-1.14±0.73	-23.29±0.49	p <0.001	-1.14±0.32	NS	p <0.001
$\triangle HR$	2.06±0.98	20.29±1.31	p <0.001	21.83±1.39	p <0.001	NS
$\triangle mBP$	-2.10±1.09	4.79±1.23	p <0.001	10.16±1.80	p <0.001	p <0.005
$\triangle sBP$	-3.86±1.31	7.40±1.69	p <0.001	13.14±2.19	p <0.001	p <0.005
$\triangle dBP$	-0.34±1.43	2.17±1.31	NS	7.17±2.12	p =0.001	p <0.05
MV	21.59±1.11	35.53±1.63	p <0.001	34.42±2.52	p <0.001	NS

Values are presented as mean ±SEM. Units of MV, BP, HR, and SaO_2 are L/min, mmHg, beats/min, and percent of Hb saturation with O_2, respectively. St. Dif: statistical difference; N: normoxia; NS: nonsignificant.

Table II. Correlations between $\triangle mBP$ and $\triangle SaO_2$, $\triangle HR$, and MV during hypoxic and exercise conditions.

Parameter		$\triangle mBP$ *vs* $\triangle SaO_2$	$\triangle mBP$ *vs* $\triangle HR$	$\triangle mBP$ *vs* MV
Hypoxia	Correlation	-0.22	0.30	0.05
	p value	NS	p <0.05	NS
Exercise	Correlation	-0.15	0.57	0.47
	p value	NS	p <0.001	p <0.005

MV is minute ventilation and $\triangle SaO_2$, $\triangle HR$, and $\triangle mBP$ are changes in arterial oxygen saturation, heart rate, and mean blood pressure relative to those of resting conditions.

sphygmomanometer (Model AOS-10, Roland, Germany), and minute ventilation (MV) using a spirometer.

Data analysis

Minute ventilation measured during the last minute of three experimental conditions and the differences in SaO_2, HR, and BP between the last minute of experimental conditions and those of rest were calculated and expressed as mean±SEM. The data of three experimental conditions were compared with each other using paired "t" test. Linear regression analysis between data was performed by the least square method. Significance was accepted at $p<0.05$.

RESULTS

Oxygen saturation

The $\triangle SaO_2$ in hypoxic condition (-23.29±0.49) was significantly lower than those of normoxic (-1.14±0.73) and exercise (-1.14±0.32) conditions ($p<0.001$ for both cases). However, there was no significant difference in $\triangle SaO_2$ between exercise and normoxic conditions (Table I).

Heart rate

The $\triangle HR$ in both hypoxic (20.29±1.31) and exercise (21.83±1.39) conditions was significantly higher than that of normoxic condition (2.06±0.98) ($p<0.001$ for both cases). However, $\triangle HR$ was not significantly different between hypoxic and exercise conditions (Table I).

Minute ventilation

The MV in both hypoxic (35.53±1.63) and exercise (34.42±2.52) conditions was significantly higher than that of normoxic condition (21.59±1.11) ($p<0.001$ for both cases). However, MV was not significantly different between hypoxic and exercise conditions (Table I).

Blood pressure

The changes in both systolic and mean blood pressure in hypoxic and exercise conditions were significantly higher than that of normoxic condition ($p<0.001$ for all cases), but $\triangle dBP$ was higher than normoxic condition only in the exercise condition ($p=0.001$). The $\triangle mBP$, $\triangle sBP$, and $\triangle dBP$ were also significantly higher in exercise than those of hypoxic condition ($p<0.005$ for $\triangle mBP$ and $\triangle sBP$ and $p<0.05$ for $\triangle dBP$) (Table I).

Relationshp between △mBP and other parameters

There was a weak but significant relationship between △mBP and △HR ($r=0.30, p<0.05$) in the hypoxic condition. There were also significant relationships between △mBP and both △HR ($r=0.57, p<0.001$) and MV ($r=0.47, p<0.005$) in the exercise condition (Table II, Fig. 1).

DISCUSSION

The results of the present study have shown increased mean, systolic and diastolic blood pressures during hypoxia compared to normoxic conditions, while arterial O_2 saturation was reduced during hypoxia (Table I).

Many studies including those of Van Den Aardweg et al. on normal subjects,[5] Fletcher et al. on rats,[15] and Iwase et al. on dogs[4] showed that the main factor responsible for increased BP during hypoxia is reduction in SaO_2. In fact, reduction of SaO_2 stimulates the arterial chemoreceptor, and this results in increased systemic vascular resistance[16] via sympathetic stimulation and elevation of plasma catecholamines.[17]

According to the physiologic principle, another factor causing elevation of BP is increased HR leading to elevated cardiac output. We therefore compared the hypoxic condition with an exercise condition with a similar rise in HR. The data of the present study showed that during exercise the mean BP was significantly elevated, while there was no reduction in SaO_2. The heart rate and minute ventilation were also increased during both hypoxic and exercise conditions similarly. In addition, there was a weak but significant correlation between change in HR and mean BP during hypoxia and a stronger relationship during exercise condition (Table II). These results suggest that although the change in SaO_2 might influence BP in OSA patients, it is not the only factor causing increased BP during hypoxia and under experimental conditions in the present study, and change in HR is a more powerful factor for elevated BP.

Ringler et al.[8] and Okabe et al.[18] also demonstrated that in patients with OSA, arterial hypoxemia is not the main factor in increasing BP during apnea and other factors may play an important role in this phenomenon. Okabe et al.[18] and Garpested et al.[19] also demonstrated that the BP response to a change in SaO_2 during awakening and in different stages of sleep are not similar, indicating that other factors contribute to BP change during apnea in patients with OSA. In fact, Guilleminanault et al.[14] showed a coincidence of increase in HR and BP in patients with OSA. Van Den Aardweg et al.[5] also showed an increased HR in most of their subjects during hypoxia, although there was some variation between subjects in this regard.

Although the present study was performed in normal subjects and there may be some differences in the cardiocirculatory response to hypoxia between normal subjects and patients with OSA. Van Den Aardweg et al.[5] showed that in normal subjects, repetitive apnea accompanied with hypoxia can cause an elevation of BP. Iwase and co-workers[4] also showed that a reduction in SaO_2 in anesthetized dogs due to repetitive airway obstruction caused a rise in BP.

It might be thought that the airway obstruction itself during apnea in OSA patients influences the cardiocirculatory response during hypoxia. However, Iwase et al.[4] demonstrated that airway occlusion without a reduction in SaO_2 (administering pure O_2 during airway occlusion) did not lead to an elevation of BP, while hypoxic exposure without airway occlusion caused a rise in BP, confirming that airway occlusion during hypoxia does not influence the cardiocirculatory response. The data of the present study also indicated that both hypoxia and exercise, in the absence of airway obstruction, caused increased blood pressure.

Another possible factor influencing the change of BP in patients with OSA during hypoxia is a specific response related to sleep in these patients. The study of Okabe et al.[18] showed that elevation of BP in response to intermittent hypoxia while awake is less than during apneic episodes while asleep. Garpested et al.[19] also demonstrated that sleep stage alters the hemodynamic response to obstructive apnea during sleep. However the studies of Iwase et al.[4], Okabe et al.[18], and Garpested et al.[19] did not assess the contribution of change in HR on elevation of BP during hypoxia.

The changes in systolic, diastolic and mean BP in the present study were also significantly higher during exercise that hypoxic conditions, while the change in HR was similar. The cause of this discrepancy is perhaps as follows: during hypoxia, increased HR and perhaps chemoreceptor stimulation and the autonomic nervous system tend to elevate BP. On the other hand, the local vascular effect of hypoxia is inhibitory and tends to reduce BP by vasodilation[20] However, because the hypoxic vascular effect is detected only in severe hypoxia, the hypoxia produced in the present study may have been insufficient to induce a significant local vascular effect. During exercise, however, the absence of hypoxia and local vascular effect leads to a greater elevation of BP than hypoxic conditions.

Previous reports have shown a link between the ventilatory response and the hemodynamic response to hypoxia.[18,21] The present study also showed a similar link during both hypoxia and exercise (Tables I and II) which suggests that ventilatory and hemodynamic responses to hypoxia are at least partially modulated by common mechanisms, perhaps via stimulation of peripheral chemoreceptors.

The results of our study also indicated that change in negative intrathoracic pressure leading to increased left ventricular transmural pressure, respiratory acidosis, arousal from sleep and interruption of ventilation do not contribute in the hemodynamic response to hypoxia which is in agreement with a previous report.[4]

In conclusion, the results of the present study indicated

that under experimental conditions, increased HR affects the elevation of BP during hypoxia, and changes in negative intrathoracic pressure, respiatory acidosis, arousal from sleep and interruption of ventilation do not contribute to this phenomenon, although there may be some differences between normal subjects and patients with OSA regarding the effect of a change in SaO_2 and HR on BP.

REFERENCES

1. Guilleminanault C, Simmons FB, Motta J, Cummiskey J, Rosekind M, Schroeder JS, Dement WC: Obstructive sleep apnea syndrome and tracheostomy: long term folllow-up experience. Arch Intern Med 141: 985-988, 1981.
2. Sforza E, Capecchi V, Lugaresi E: Haemodynamic effects of short-term nasal continuous positive airway pressure therapy in sleep apnea syndrome: monitoring by a finger arterial pressure device. Eur Respir J 5: 858-863, 1992.
3. Palomaki H, Partinen M, Juvela S, Kaste M: Snoring as a risk factor for sleep related brain infarction. Stroke 20: 1311-1315, 1989.
4. Iwase N, Kikuchi Y, Hida W, Miki H, Taguchi O, Satoh M, Okabe S, Takishima T: Effect of repetitive airway obstruction on O_2 saturation and systemic and pulmonary blood pressure in anaesthetized dogs. Am Rev Respir Ds 146: 1402-1410, 1992.
5. Van Den Aardweg JG, Karemaker JM: Repetitive apneas induce periodic hypertension in normal subjects through hypoxia. J Appl Physiol 72: 821-827, 1992.
6. Tolle FA, Judy WV, Yu P, Markland ON: Reduced stroke volume related to pleural pressure in obstructive sleep apnea. J Appl Physiol 55: 1718-1724, 1983.
7. Richardson DW, Wasserman AJ, Patterson JLJr: General and regional circulatory response to change in blood pH and carbon dioxide tension. J Clin Invest 40: 31-43, 1961.
8. Ringler J, Basner RC, Shanon R, Schwartzstein R, Manning H, Weinberger SE, Weiss JW: Hypoxemia alone does not explain blood pressure elevations after obstructive apnea. J Appl Physiol 69: 2143-2148, 1990.
9. Krieger J, Follenius M, Sforza E, Brabdenberger G, Peter JD: Effects of treatment with nasal continuous positive airway pressure on atrial natriuretic peptide and arginine vasopressin release during sleep in patients with obstructive sleep apnea. Clin Sci Lond 80: 443-449, 1991.
10. Shepard WE Jr: Gas exchange and hemodynamics during sleep. Med Clin North Am 69: 1243-64, 1985.
11. Schroeder JS, Motta J, Guilleminanault C: Hemodynamic studies in sleep apnea. In: Guilleminanault C, Dement WC, (eds.), Sleep Apnea Syndromes, New York: Liss, pp. 177-196, 1978.
12. Blumberg H, Janig W, Rieckmann C, Szulczyk P: Baroreceptor and chemoreceptor reflexes in postganglionic neurones supplying skeletal muscle and hairy skin: J Auton Nerv Syst 2: 223-240, 1980.
13. Somer VK, Mark AL, Abboud FM: Synergic sympathetic activation by hypercapnic hypoxia–implications for sleep apnea. Proc 12th Sci Mtg Int Soc Hypertens p. 1182, 1988.
14. Guilleminanault C, Conolly S, Wienkle R, Melvin K, Tilkian A: Cyclical variation of the heart rate in sleep apnea syndrome. Lancet 1: 126-131, 1984.
15. Fletcher EC, Lesske J, Behm R, Miller CC, Stauss H, Unger T: Carotid chemoreceptor, systemic blood pressure, and chronic episodic hypoxia mimicking sleep apnea. J Appl Physiol 72: 1978-1984, 1992.
16. Downing SE, Mitchel JH, Walace AG: Cardiovascular response to ischemia, hypoxia, and hypercapnia of the central nervous system. Am J Physiol 204: 881-887, 1963.
17. Fletcher EC, Miller J, Schaaf JW, Fletcher JG: Urinary catecholamine before and after tracheostomy in patients with obstructive sleep apnea and hypertension. Sleep 10: 35-44, 1987.
18. Okabe S, Hida W, Kikuchi Y, Taghuchi O, Ogawa H, Mizusawa A, Miki H, Shirato K: Role of hypoxia on increased blood pressure in patients with obstructive sleep apnea. Thorax 50: 28-34, 1195.
19. Garpested E, Ringler J, Parker JA, Remsburg S, Weiss JW: Sleep stage influences the hemodynamic response to obstructive apnea. Am J Respir Crit Care Med 152: 199-203, 1995.
20. Daugherty RM Jr, Scott JB, Dabney JM, Haddy FJ: Local effects of O_2 and CO_2 on limb, renal and coronary vascular resistance. Am J Physiol 213: 1102-1110, 1967.
21. Hender JA, Wilcox I, Laks I, Grunstein RR, Sullivan CF: A specific and potent pressor effect of hypoxia in patients with sleep apnea. Am Rev Respir Dis 146: 1402-10, 1992.