MECHANISMS OF CHANGES IN ARTERIAL PRESSURE AND HEART RATE IN ACUTE HYPOXIC HYPOXIA

L. I. Ardashnikova

UDC 616-008.922.1.04-07:616.12-008.3-07

The chemoreceptors of the carotid sinus, which are of extreme importance in the regulation of respiration, are found to play a less important role in the regulation of the circulation during hypoxemia.

* * * *

It became clear as a result of the work of Heymans [11], and his collaborators that the responses of the respiratory and cardiovascular systems directed toward adaptation to hypoxia are brought about by excitation of the chemoreceptors of the carotid and cardio-aortic zones. It was considered that a low partial pressure of oxygen (pO_2), which is an adequate stimulus for these chemoreceptors, produces not only an increase in the minute volume of respiration (MVR) but also an increase in arterial pressure (AP), and an increase in the heart rate. In recent years, however, findings have been described indicating that excitation of chemoreceptors produces inconsistent and relatively slight changes in the cardiovascular system [2, 3, 13]. The evidence of onset of reflex bradycardia during hypoxia previously described in the literature [7] has been confirmed and developed [6, 8, 14]. Under hypoxic conditions an increase in MVR takes place only because of excitation of the chemoreceptors [1, 5], whereas changes in the cardiovascular system may be dependent on other factors also. According to some data [8, 13], for instance, the increase in the heart rate is due to reflex influences from the receptors of the lungs, whose excursion is increased in hypoxia. The hypocapnia developing during hyperventilation is also known to have some effect on the state of the cardiovascular system [10, 11].

The object of the present investigation was to make an experimental analysis of the importance of excitation of the chemoreceptors, of an increase in MVR, and of hypocapnia in the changes in AP and heart rate developing during hypoxia.

EXPERIMENTAL METHOD

Experiments were performed on cats anesthetized with urethane (0.8-1 μg/kg). Recordings were made of the MVR, pneumogram, impulse activity in the diaphragm, AP in the femoral artery, and pulse rate (from the ECG). Before the experiment began both depressor nerves were divided at the point where they leave the laryngeal nerve. As far as possible in each experiment the same animals successively breathed a mixture deficient in oxygen (7%) under different conditions (Table 1). In variants 1 and 2, during natural respiration, an increase in MVR took place, accompanied in variant 1 by hypocapnia, which was prevented in variant 2 by the addition of 3% CO_2 to the inhaled gas mixture. In variants 3, 4, and 5 of the experiment, hypoxemia was produced against a background of artificial respiration with regulation of the MVR.

In variant 3, the MVR was maintained at the initial level, but in variants 4 and 5 at an elevated level approximately the same as that found under hypoxic conditions during natural respiration. The hypocapnia arising in variant 4 was compensated in variant 5 by the addition of CO_2. Hence, the importance of hypocapnia, the MVR being equal, could be determined by comparing the results obtained in variants 1 and 2, and in variants 4 and 5 respectively, and the importance of an increase in MVR could be determined, the CO_2 level being the same, by comparing the results obtained in variants 3, 2, and 5 of the experiment.

Laboratory of Physiology and Pathology of Respiration and Circulation, Institute of Normal and Pathological Physiology, Academy of Medical Sciences of the USSR, Moscow (Presented by Academician V. V. Parin). Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 65, No. 3, pp. 25-29, March, 1968. Original article submitted June 21, 1968.

TABLE 1. Changes in Heart Rate during Hypoxia in Individual Experiments (number of cases)

Variants of experiment	No. of experiments	Time after beginning of hypoxia (in min)	Change in heart rate per minute				
			− 15 and below	− 15 − 5	− 5 + 5	+ 5 + 15	+ 15 and above
1 and 2	32	1	5	4	19	2	2
		3	13	5	6	5	3
3	34	1	7	8	17	2	0
		3	18	8	6	1	1

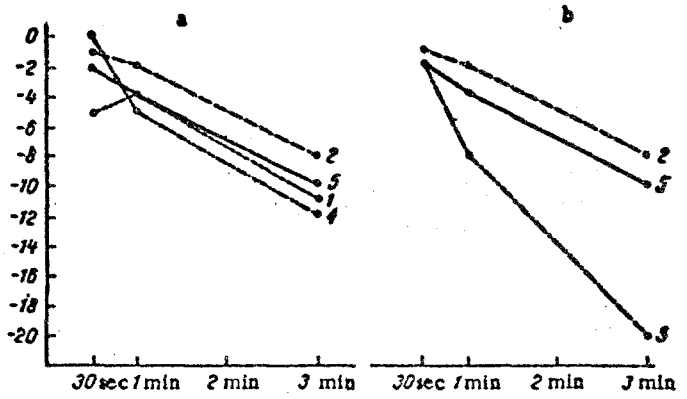

Fig. 1. Changes in heart rate during hypoxia in different variants of experiments (denoted by numbers). Abscissa, time; ordinate, changes in heart rate per minute.

EXPERIMENTAL RESULTS AND DISCUSSION

The mean values of the changes in heart rate in variants 1, 2, 4, and 5 are shown in Fig. 1a. Bradycardia developed in all these experiments, hardly perceptible in the first 30 sec of hypoxemia but relatively well marked by the third minute. Consequently, with an increase of MVR, whether with a lowered (variants 1 and 4) or a normal CO_2 level (variants 2 and 5), bradycardia developed gradually during hypoxemia. The results obtained in variants 2 and 5 are compared in Fig. 1b with those obtained in variant 3. It is clear that the bradycardia was much more marked in variant 3, i.e., under conditions excluding an increase in MVR during hypoxia. These results were confirmed by analysis of data obtained in individual experiments. As Table 2 shows, during the first minute of hypoxia in variants 1 and 2 the number of cases with slowing of the pulse was only slightly greater than the number of cases with quickening, and in most experiments no appreciable changes took place; at the third minute in most experiments bradycardia was observed, but in some experiments there were no appreciable changes and occasionally tachycardia was found.

Hence, during natural respiration bradycardia did not develop in all the experiments. In contrast to this, in variant 3 (artificial respiration without an increase in MVR) bradycardia developed in the first minute in half the experiments, and by the third minute in the overwhelming majority of experiments; an increase in pulse rate was found only as an exception (Table 1).

Consequently, during excitation of the chemoreceptors of the carotid zones by a low pO_2, bradycardia developed in most experiments. It was well marked when the MVR remained constant and was much less marked when the MVR increased, usually in association with hypoxemia. The presence or absence of hypocapnia under these experimental conditions had no significant effect on the results.

The changes in AP in the same variants of the experiments are shown in Fig. 2a and b. By the 30th second of hypoxemia the mean value of the AP was slightly raised in all variants of the experiments. This was evidently a manifestation of a pressor reflex from the carotid sinus chemoreceptors. However, by the end of the first minute the changes in AP had become less consistent. By the 3rd minute a distinct decrease in the mean value of the AP was observed in all variants of the experiments, reaching a mean value of 6-13 mm in the different variants. As Table 2 shows, the changes in AP in different experiments were

TABLE 2. Changes in AP during Hypoxia in Individual Experiments (number of cases)

No. of experiments	Time (in min)	Changes in AP (in mm)				
		less than −15	−15 − 5	−5 + 5	+5 + 15	+15 and over
95	1	5	23	36	25	6
	3	35	24	23	14	1

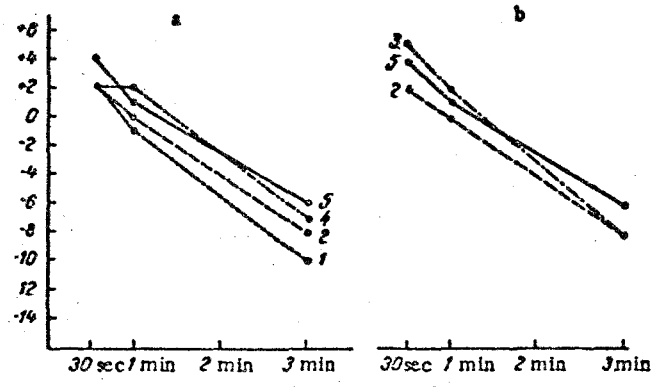

Fig. 2. Changes in arterial pressure during hypoxia in different variants of experiments. Abscissa, time; ordinate, changes in arterial pressure (in mm).

unequal in the first minute: in many experiments the AP was unchanged, in others it was lowered, and in some it was raised. By the 3rd minute the number of experiments in which the AP was lowered was much greater than the number of experiments with an increased AP. However, an increase in AP was still occasionally observed (Table 2).

Hence, the changes in AP during hypoxia are variable in direction, with an appreciable, although small, predominance of a decrease toward the end of the 3rd minute.

As Fig. 2a shows, the AP decreased toward the end of the 3rd minute in all variants of the experiments. In experiments with compensation of the hypocapnia, it was rather less marked (in variant 2 compared with variant 1 and in variant 5 compared with variant 4). However, this difference was not significant. It should, therefore, be accepted that under these experimental conditions hypocapnia played no significant role in the lowering of the AP. The decrease in AP toward the end of the 3rd minute was less marked in variants 2 and 5 in which the MVR was increased. This may have been connected with the compensatory effect of hyperventilation under hypoxemic conditions.

It may be concluded from the results obtained that, in contrast to the reflex changes in respiration, considerable in magnitude and uniform in direction, observed in our experiments under the influence of hypoxemia (the increase in MVR amounted to 40-60%, the amplitude of the respiratory movements on the pneumogram and the electrical activity of the diaphragm were always increased), the changes in heart rate and AP were small and were often divergent, especially in the 1st minute, when the reflex factor associated with excitation of the chemoreceptors was manifested in its purest form. The pressor effect of excitation of chemoreceptors, evidence of which had been obtained by perfusion of the isolated carotid sinuses with blood with a low pO_2 [9, 12], is only slight under conditions of general hypoxia and raises the AP for a short time, after which it soon falls again. In milder degrees of hypoxia the pressor effect may possibly be more stable [14].

The decrease in AP arising at the 3rd minute of hypoxemia cannot be explained by any of the three factors considered above (excitation of chemoreceptors, hypocapnia, increase of MVR). It may be postulated that it is the result of local vasodilatation under the influence of generalized hypoxia or that it reflects the direct effect of hypoxia on the vasomotor center [11]. It should be noted that the level of hypoxemia

created in these experiments (7-7.5% oxygen in the inspired gas mixture) may be regarded as severe, although it did not cause inhibition of the respiratory center. The reflex increase in respiration, in association with the direct effect of this degree of hypoxemia on the central nervous system, thus took place to the full, whereas the pressor effect of stimulation of the chemoreceptors did not prevent a decrease of AP. Consequently, the role of the chemoreceptors in regulation of the AP under conditions of general and acute hypoxemia is not so decisive as in the regulation of respiration. The reflex bradycardia due to stimulation of chemoreceptors under conditions when the MVR was artificially maintained constant was fairly well marked, but under ordinary conditions, when the MVR increased under the influence of hypoxemia, bradycardia took place only in some experiments, and it rarely attained a considerable magnitude.

In face of the results obtained by perfusion of the isolated carotid sinus [9-11], it may be considered that the bradycardia during general hypoxemia is caused by excitation of the chemoreceptors. However, the fact that it was more marked at the 3rd minute of hypoxemia than at the first, and that it developed at the time when the AP was beginning to fall suggests that the direct action of hypoxia on the centers of cardiac innervation may be concerned, along with the chemoreceptors of the carotid body, in the mechanisms of its origin.

LITERATURE CITED

1. L. I. Ardashnikova, In: Oxygen Therapy and Oxygen Lack [in Russian], Kiev (1952), p. 77.
2. L. I. Ardashnikova, Abstracts of Scientific Proceedings of the Tenth Congress of the I. P. Pavlov All-Union Physiological Society [in Russian], Vol. 2, No. 1, Moscow-Leningrad (1964), p. 50.
3. L. I. Ardashnikova, Byull. Éksp. Biol., No. 4, 3 (1966).
4. M. E. Marshak, L. I. Ardashnikova, G. N. Aronova, et al., In: Regulation of Respiration, the Circulation, and Gas Exchange [in Russian], Moscow (1948), p. 65.
5. M. E. Marshak, Regulation of Respiration in Man [in Russian], Moscow (1961).
6. I. S. Ugolbaeva, Byull. Éksp. Biol., No. 9, 34 (1964).
7. T. Bernthal, W. Greene, Jr., and A. M. Revzin, Proc. Soc. Exp. Biol. (New York), 76, 121 (1951).
8. M. de. B. Daly and M. J. Scott, J. Physiol. (London), 144, 148 (1958).
9. S. E. Downing and J. H. Siegel, Am. J. Physiol., 204, 471 (1963).
10. E. Gellhorn, Regulatory Functions of the Autonomic Nervous System [Russian translation], Moscow (1948).
11. C. Heymans and D. Cordier, The Respiratory Center [Russian translation], Moscow-Leningrad (1949).
12. C. Heymans and E. Neil, Reflexogenic Areas of the Cardiovascular System, London (1958).
13. P. I. Korner, J. Physiol. (London), 180, 279 (1965).
14. R. D. M. MacLeod and M. J. Scott, J. Physiol. (London), 175, 193 (1964).