PHRENIC BLOOD FLOW IN HYPOXIA AND HYPERCAPNIA

N. V. Sanotskaya, D. D. Matsievskii, and S. O. Aleinikov

UDC 616.152.21-008.64-07:616.26-005

KEY WORDS: phrenic artery; blood flow; hypoxia; hypercapnia; ultrasound

Data on changes in the blood supply to the respiratory musculature during hypoxia and hypercapnia are contradictory. A twofold increase in the phrenic blood flow has been noted, when pulmonary ventilation was doubled during hyperventilation caused by hypercapnia [7]. An increase in the phrenic blood flow by only 25% was observed when ventilation of the lungs was doubled in dogs inhaling a hypoxic-hypercapnic gas mixture [10, 11]. It has been shown on dogs that the blood flow in the diaphragm increases as a linear function with an increase in respiratory work caused by hyperventilation arising under the influence of hypercapnia [8, 9]. The results of other investigations have shown that a four-fivefold increase in ventilation of the lungs can cause a 10-20-fold increase in blood supply of the respiratory muscles [5, 6, 8, 9], or in other words, it has been shown that the blood supply of the respiratory musculature increases by a greater degree than the increase in pulmonary ventilation. In previous studies the results were directly opposite: the blood supply of the respiratory muscles was increased less than the increase in work of the respiratory musculature, expressed as the value of the pulmonary ventilation.

The aim of this investigation was to study changes in the phrenic blood flow and their correlation with changes in pulmonary ventilation in the presence of different degrees of hypoxia and hypercapnia.

EXPERIMENTAL METHOD

The following parameters were studied in acute experiments on 20 male and female cats weighing 2-4 kg under pentobarbital (40-50 mg/kg, intraperitoneally) anesthesia: the linear and volume velocity of the blood flow in the left phrenic artery (PA) by an ultrasonic method [1], the resistance of the vascular bed of PA and the arterial blood pressure in the femoral artery (BP) by means of a micromanometer [2], and the respiratory excursions of the lower part of the chest during different degrees of exposure to hypoxia and hypercapnia, during asphyxia and, in some experiments, after acute blood loss. The blood flow was measured by means of miniature bandage-type transducers 0.3 and 0.5 mm in diameter, working at an ultrasonic frequency of 26.8 MHz. Data relating to blood flow and BP were led into an analog minicomputer to calculate the resistance of the vascular bed of PA in real time. The method of studying blood flow along PA was described by the writers previously [4]. The experiments were carried out without opening the peritoneal cavity, and with the animal breathing spontaneously. To create conditions of hypoxic hypoxia and hypercapnia, gas mixtures of the following composition were used: 10, 7.5, 5, and 3% O_2 in nitrogen; 3, 5, and 7% CO_2 in air. The gas mixtures were administered to the animal through a valve for 3-5 min, with an interval

Laboratory of Pathophysiology of Respiration and Bioengineering Laboratory, Institute of General Pathology and Pathological Physiology, Russian Academy of Medical Sciences, Moscow. (Presented by Academician of the Russian Academy of Medical Sciences A. G. Chuchalin.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 114, No. 12, pp. 580-583, December, 1992. Original article submitted March 4, 1992.

 0007-4888/92/0012-1758$12.50

TABLE 1. Arterial Blood Gases During Inhalation of Gas Mixtures of Different Composition (M ± m)

Gas mixture	p_aO_2, mm Hg	P_aCO_2, mm Hg	pH
Atmospheric air	96,39 (±2,86)	42,83 (±1,95)	7,39 (±0,03)
10 % O_2	63,01 (±1,35)	26,9 (±0,82)	7,37 (±0,01)*
7,5 % O_2	56,17 (±0,91)	22,73 (±1,2)	7,45 (±0,01)*
5 % O_2	27,52 (±1,28)	19,65 (±1,2)	7,48 (±0,01)
3 % O_2	17,8 (±1,25)	18,4 (±1,3)	7,55 (±0,01)
3 % CO_2	103,58 (±0,83)	43,5 (1,72)*	7,34 (0,01)*
5 % CO_2	109,5 (±0,9)	50,28 (±1,57)	7,31 (±0,01)
7 % CO_2	113,3 (±1,1)	55,3 (±1,2)	7,27 (±0,02)

Legend. *p > 0.05 compared with initial data.

of 15-20 min. The mixtures were usually given to the animal in order of increasing hypoxia – from 10% to 3% O_2, and hypercapnia – from 3 to 7% CO_2. Acute blood loss was caused by bleeding from the femoral artery to an amount of 20-30% of the circulating blood volume. The lost blood was restored by intravenous infusion. The tidal volume and the arterial blood gases (p_aO_2, p_aCO_2, pH) were measured by the Astrup–Siggard–Andersen method (Table 1).

EXPERIMENTAL RESULTS

Inhalation of gas mixtures with a reduced oxygen concentration caused the resistance of the vascular bed of PA to decrease and the blood flow along PA to increase, but not always proportionally to the degree of hypoxia. Inhalation of a gas mixture containing 10% O_2 caused an increase in the linear velocity of the blood flow along PA on average to 153%, and of the volume velocity of the blood flow to 202%, whereas the resistance of the vascular bed of PA was reduced by 58% of its initial level (Fig. 1a). The tidal air volume under these circumstances rose to 140% of the initial level. During inhalation of a mixture containing 7.5% O_2 the linear velocity of the blood flow rose on average to 134%, and the volume velocity to 149%, whereas resistance fell to 67% of the initial level. The tidal air volume rose to 175%. During inhalation of a mixture containing 5% O_2 the degree of increase of the blood flow and decrease of the resistance of the vascular bed of PA was considerably greater than in response to inhalation of 10 and 7.5% O_2 the linear velocity rose to 241% and the volume velocity to 287%, while the vascular resistance of PA fell to 39%. The tidal air volume rose to 200%. It will be noted that more moderate hypoxia (10% O_2) caused a greater increase of blood flow along PA than inhalation of the more deprived gas mixture containing only 7.5% O_2 Meanwhile the tidal air volume at 10% O_2 increased rather more. Evidently during inhalation of 7.5% O_2 the contribution of the external intercostal muscles to the total lung ventilation increased. Another possibility is that during the transition from inhalation of a gas mixture with 10% O_2 to a mixture with 7.5% O_2 the metabolic demands of the diaphragm were satisfied not so much by an increase in its blood supply as by an increase in the arteriovenous oxygen difference. Under even harsher conditions of hypoxia (5% O_2) both mechanisms of satisfying the metabolic demands were evidently involved: both a marked increase in the blood flow and greater extraction of oxygen from the inflowing blood.

Inhalation of a gas mixture. containing 3% O_2 caused the linear velocity of the blood flow to rise to 300% and volume velocity to 385%, whereas the resistance of the vascular bed of PA fell to 30%. The tidal air volume increased to 230% of its initial value, i.e., all the parameters exceeded values found during inhalation of a gas mixture with 5% O_2.

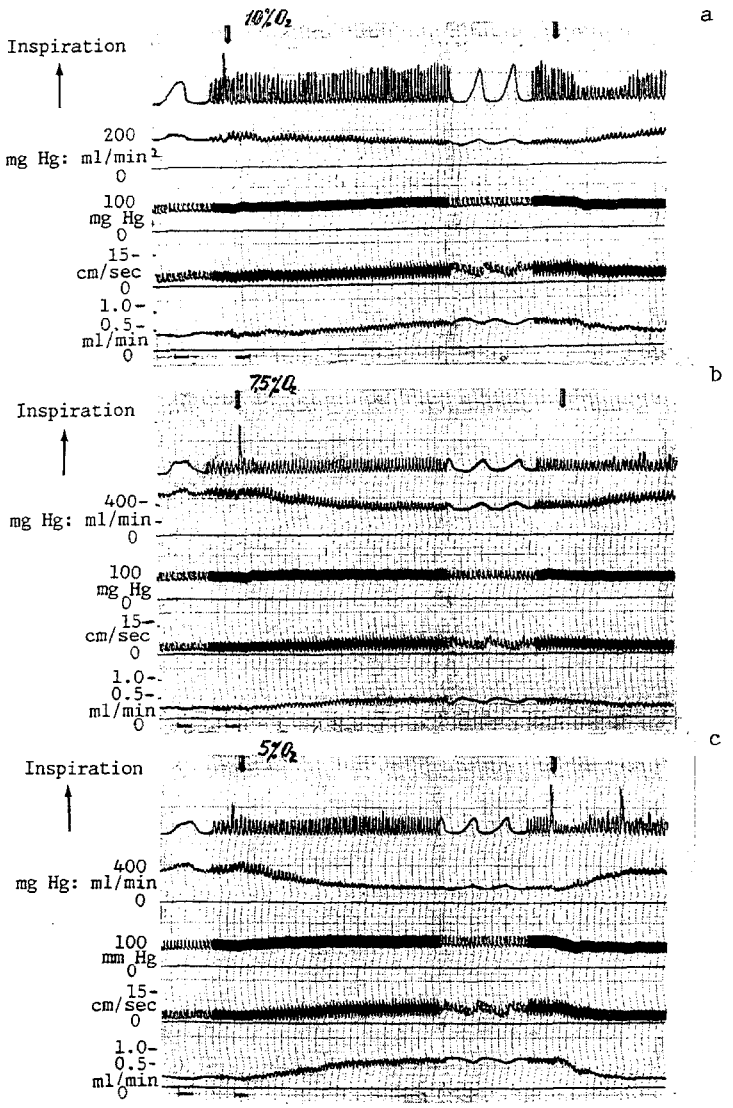

Fig. 1. Changes in resistance of vascular bed of phrenic artery (PA) and blood flow along PA at different degrees of hypoxia: a) inhalation of gas mixture containing 10% O_2; b) 7.5% O_2; c) 5% O_2. From top to bottom: respiration, resistance of vascular bed of PA, blood pressure in femoral artery, linear velocity of blood flow in PA, volume velocity of blood flow in PA. Here and in Figs. 2 and 3: thin lines beneath each curve are zero levels. Arrows indicate beginning and end of inhalation of gas mixture. Time scale 10 and 1 sec.

During inhalation of gas mixtures with an increased CO_2 concentration the blood flow along PA increased proportionally to the degree of hypercapnia up to a certain level of p_aCO_2. A mixture containing 3% CO_2 caused the linear velocity of the blood flow to rise on average to 172% and the volume velocity to 222%, whereas the vascular resistance of PA fell to 53.7% of its initial level (Fig. 2a). Pulmonary ventilation rose to 235%. In the presence of 5% CO_2 the linear velocity of the blood flow rose to 239% and the volume velocity to 329%, whereas the vascular

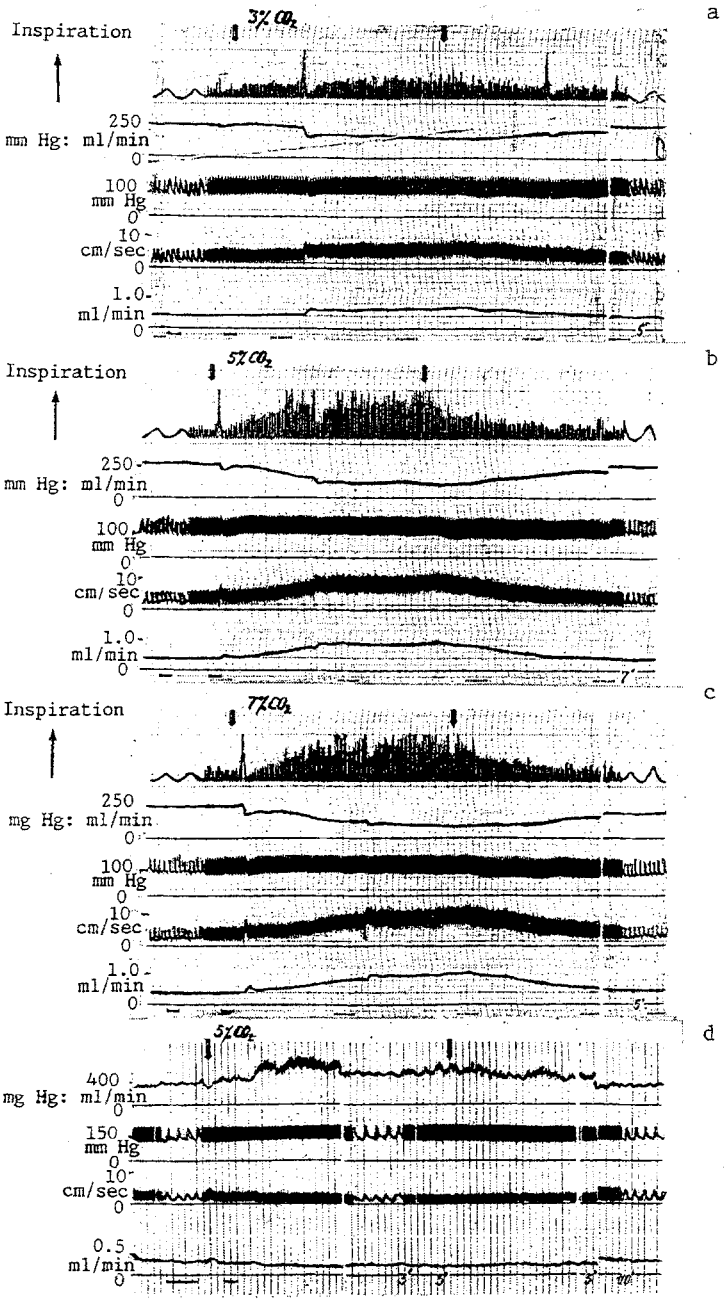

Fig. 2. Changes in resistance of vascular bed of PA and blood flow along PA at different degrees of hypercapnia: a) inhalation of gas mixture containing 3% CO_2; b) 5% CO_2; c) 7% CO_2; d) 5% CO_2 with artificial respiration. Significance of curves (for a, b, c) as in Fig. 1. For d, resistance of vascular bed of PA, BP in femoral artery, linear velocity of blood flow in PA, volume velocity of blood flow in PA. Time scale 10 and 1 sec.

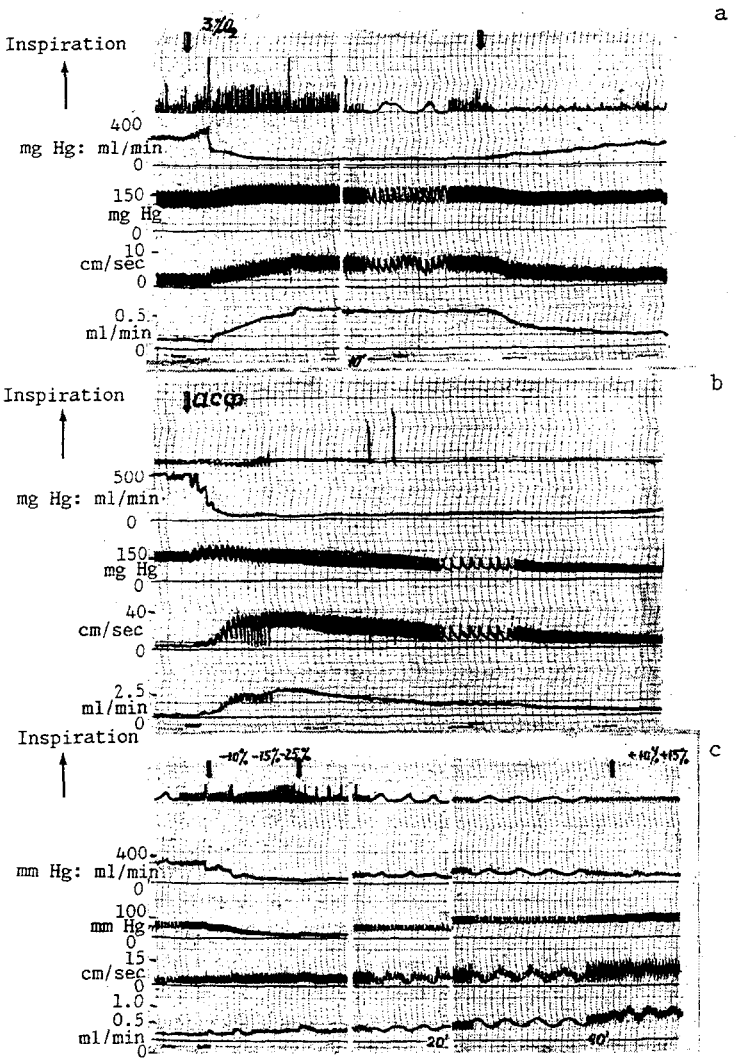

Fig. 3. Changes in resistance of vascular bed of PA and blood flow along PA during inhalation of gas mixture containing 3% O_2 (a), during asphyxia (b), and acute blood loss (c). Significance of curves as to Figs. 1 and 2. Time scale 10 and 1 sec. Arrows indicate beginning and end of inhalation of gas mixture and blood loss (for a and c), for b) beginning of asphyxia. For c) figures with minus sign denote blood loss in ml; with plus sign – intravenous infusion of blood.

resistance of PA fell to 35% of the initial level (Fig. 2b); the tidal air volume to 350%. Thus during the switch from inhalation of a gas mixture with 3% to one with 5% CO_2 the response of the blood flow increased proportionally to the degree of hypercapnia and of ventilation of the lungs. However, inhalation of a mixture containing 7% CO_2 caused a smaller reaction than a mixture with 5% CO_2; the linear velocity rose to 213% and volume velocity to 256%, whereas the resistance of the vascular bed of PA fell to 46% of the initial level (Fig. 2c). Meanwhile the pulmonary ventilation rose to 420%. It can be tentatively suggested that just as during inhalation of 7.5% O_2, during inhalation of 7% CO_2 the respiratory musculature of the chest played a more active role in ventilation of the lungs. It is also possible that this fact may be linked with the vasoconstrictor action of high CO_2 concentrations on the

vascular bed of PA. This is suggested by the results of experiments conducted under artificial respiration, during inhalation of gas mixtures with an increased CO_2 concentration. In this case hypercapnia caused an effect opposite to that taking place during natural breathing, namely an increase in resistance of the vascular bed of PA and a decrease in the blood flow (Fig. 2d). With the diaphragm in a passive state, due to the artificial ventilation, hypercapnia had a vasoconstrictor effect on PA. Evidently if the CO_2 concentration in the inspired air is high, summation takes place of the vasodilator effect due to the high metabolic demands of the diaphragm, as a result of its increased work, and the vasoconstrictor effect (probably neurogenic): summation of the local and reflex effect of hypercapnia takes place, as has been shown for skeletal muscle [3].

Changes in the blood flow and vascular resistance of PA during inhalation of a mixture containing 5% O_2 (Fig. 1c) and 5% CO_2 (Fig. 2b) are comparable (close to threefold). Meanwhile the tidal air volume at 5% CO_2 rose significantly more (by 3.5 times) than during inhalation of 5% O_2 (twofold). During hypoxia the increased ventilation of the lungs must be guaranteed when the oxygen supply brought by the blood is reduced. That is why the smaller increase in pulmonary ventilation during hypoxia must be produced by a higher blood flow than the greater increase in ventilation associated with hypercapnia. The reduced p_aO_2 evidently has a direct vasodilator action on the vascular bed of PA.

Thus the ratio of the degree of increase in pulmonary ventilation and the increase in the phrenic blood flow depends on the character of the factors to which the diaphragm is exposed.

The behavior of the vascular bed of PA under certain extremal situations, such as very severe hypoxia (3% O_2), prolonged asphyxia, and acute blood loss, is particularly interesting. During inhalation of a gas mixture containing 3% O_2, the respiratory movements are increased in amplitude and frequency and, as has already been stated, the blood flow along PA is increased and the vascular resistance of PA reduced. After inhalation of this mixture has ceased, probably as a result of the development of hypocapnia, the respiratory movements are sharply reduced. Meanwhile the blood flow along PA remains for a long time at a higher level than initially, whereas the vascular resistance is reduced (Fig. 3a). This is connected with liquidation of the oxygen debt of the diaphragm which arose during hypoxia, not with the current metabolic demands, for the respiratory movements are inhibited and lung ventilation is depressed.

During long-term asphyxia, continuing until respiratory arrest, the blood flow to the diaphragm remains at a high level, even after cessation of the respiratory movements, but later it changes parallel with the changes in BP, and the resistance of the vascular bed of PA remains low until the end of the experiment (Fig. 3b). In this case we are dealing not with the satisfying of metabolic demands, for the diaphragm is not yet contracting, but the state of readiness of the vascular bed of PA to resume an adequate blood supply to the diaphragm, if this is necessary in order to meet its metabolic demands in the case of restoration of breathing.

In acute blood loss there is a sharp decrease in cardiac output and systemic BP. Meanwhile the blood flow along PA is usually increased. In some experiments it rises after a transient initial fall, but in individual experiments it is unchanged. After restoration of the circulating blood volume by intravenous infusion, the linear and volume velocity of the blood flow along PA rises above the initial level due to the lowered resistance of the vascular bed of PA which persists throughout the period of blood loss (Fig. 3c).

In all these extremal situations the vascular bed of PA behaves as vessels supplying other vitally important organs with blood, namely the heart and brain [3]. The compensatory powers of the body under extremal conditions are aimed at ensuring their preferential blood supply compared with other organs.

REFERENCES

1. D. D. Matsievskii, Byull. Éksp. Biol. Med., No. 9, 119 (1970).
2. D. D. Matsievskii, Byull. Éksp. Biol. Med., No. 3, 377 (1984).

3. N. V. Sanotskaya, "Analysis of mechanisms determining the partial pressure of oxygen in the tissues," Author's Abstract of Dissertation for the Degree of Doctor of Medical Sciences, Moscow (1975).
4. N. V. Sanotskaya and D. D. Matsievskii, Byull. Éksp. Biol . Med., No. 1, 21 (1992).
5. D. Davidson and A. R. B. Stalcup, J. Appl. Physiol., **60**, 1230 (1986).
6. M. Manohar, T. E. Goetz, L. C. Holste, et al., J. Appl. Physiol., **64**, No. 3, 1203 (1988).
7. P. Mognoni, Resp. Physiol., **20**, 171 (1974).
8. C. H. Robertson, G. H. Foster, and R. L. Johnson, J. Clin. Invest., **59**, No. 1, 31 (1977).
9. C. H. Robertson, M. A. Pagel, and R. L. Johnson, J. Clin. Invest., **59**, No. 1, 43 (1977).
10. D. F. Rochester, J. Clin. Invest., **53**, 1216 (1974).
11. D. F. Rochester and G. Bettini, J. Clin. Invest., **57**, 661 (1976).