Decrease in Cardiac Stroke Volume in Humans during Inhalations of 8% Hypoxic Gas Mixture

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The effect of 15-min inhalation of 8% hypoxic gas mixture on stroke volume was studied in 17 healthy volunteers. The parameter decreased in all volunteers who endured this exposure to the end. At the beginning of exposure the decrease in stroke volume negatively correlated with HR changes, but this correlation disappeared as hypoxia augmented. Physiological significance of stroke volume decrease during severe hypoxia is discussed.

Key Words: *hypoxia; stroke volume; cardiac output; integral body rheography*

Cardiac output (CO) determining arterial pressure (AP) and oxygen supply to tissues is essential for the maintenance of homeostasis, particularly under extreme conditions [3]. The organism adapts to such situations by modifying heart rhythm parameters, such as HR (HR), and/or cardiac stroke volume (SV) — the parameters determining CO (CO=HR×SV). Acute hypoxic exposure is an extreme exposure modifying primarily functioning of cardiovascular and respiratory systems in order to provide survival.

Cardiac output and stroke volume in hypoxia were studied for a long time in humans and animals, but there is still no universal opinion on hypoxic changes in these parameters. The increase in SV and CO in acute hypoxia [1] was not confirmed in later studies [5] of normobaric hypoxia (12.5% oxygen in hypoxic gaseous mixture), which did not lead to changes in SV in volunteers at rest. Study on isolated rat hearts [4] showed that SV decreases proportionally with increasing myocardial hypoxia. *In vivo* study of hypocapnic hypoxia showed an increase in CO and SV in rats [7].

The absence of universal opinion about changes in CO and SV in hypoxia can be explained by different conditions of studies (oxygen concentration in inhaled air, object of study, *etc.*) and by methods for evaluation of parameters (thermodilution, acetylene method, direct Fick's method). Evaluation of SV and CO in humans under conditions of hypoxia remains a problem.

MATERIALS AND METHODS

The study was carried out on 17 male volunteers (mean age 22.0±4.1 years, heigth 177±5 cm, weight 73±10 kg), non-smokers, healthy. All volunteers gave written informed consent to participation in the study. All requirements of the Helsinki Declaration were adhered to. At all stages of the experiment each volunteer was in a sound-proof box in a state of sensorimotor rest at all stages of the study. The initial basal parameters were recorded for 15-20 min during atmospheric air inhalation; hypoxic exposure consisted in 15-min inhalations of hypoxic gas mixture (8% oxygen in nitrogen). After inhalation the volunteers remained in the box for 20-25 min longer and inhaled atmospheric air (recovery). Integral body rheogram was recorded for evaluating SV and CO. Cerebral circulation volume rate was recorded by rheoencephalography in the following mode: three records of basal rheoencephalogram and integral body rheogram; integral

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body rheograms during 5th, 10th, and 15th min of hypoxia and recovery and during 20th min of recovery; rheoencephalography during hypoxia and recovery minutes 1-4, 6-9, 11-14 and recovery minutes 16-19. The duration of integral body rheography was 30-40 sec, rheoencephalography 40-45 sec. Probing current frequency in integral body rheography was 28 kHz, in rheoencephalography 115 kHz. Conditions of the study did not permit the volunteer assume a standard horizontal posture, which could modify the results of measurements. However, presumably constant sitting posture of the volunteers had the same effect on the results. We therefore used arbitrary units of SV and CO, basal values being taken for 100%. In parallel, oxygen saturation of arterial blood hemoglobin (SpO_2) was evaluated by pulse oxymetry. AP was recorded by tonometry. The means were compared by pairs using Student's *t* test; Pierson's correlation coefficients were determined. Standard Statistica 6.0 software was used. The results were considered significant at $p<0.05$.

RESULTS

Fifteen of 17 volunteers endured 15-min hypoxic exposure completely. Two volunteers asked to stop the exposure at different time of the study (during minutes 6 and 8 of hypoxia). The results for these two volunteers are not analyzed, because of insufficient data on SV and CO.

Hypoxic exposure led to a decrease in SpO_2 ($p<0.0001$) and increase in HR ($p<0.0001$; Table 1). Increases in systolic and diastolic AP were negligible (Table 1). Stroke volume decreased under the effect of hypoxia in all volunteers (Fig. 1) and was 77.4±10.2% of basal level during minute 5, 77.7±9.3% during minute 10, and 77.7±11.7% during minute 15. Stroke volume during recovery

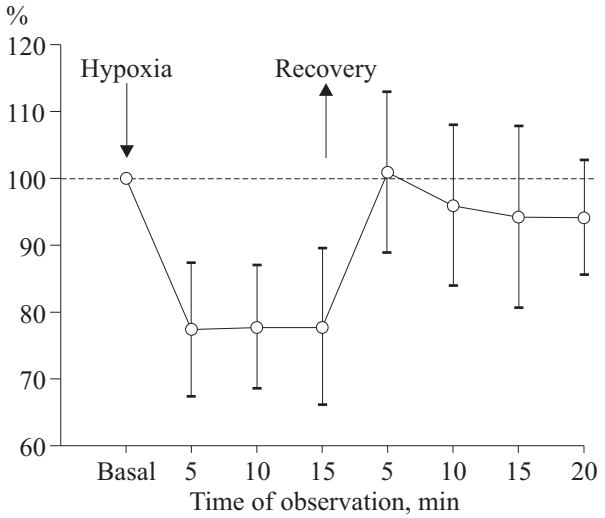

Fig. 1. Changes in stroke volume in volunteers. Ordinate: stroke volume (% of basal level).

was 100.9±12.1% during minute 5, 95.9±12.1% during minute 10, 94.2±13.5% during minute 15, and 94.1±8.6% of basal level during minute 20. During minute 5 of hypoxia and minute 5 of recovery SV changes negatively correlated with HR values ($r=-0.75$ at $p=0.002$ and $r=-0.69$ at $p=0.007$, respectively). During minute 10 and minute 15 of hypoxia no correlation between HR and SV values were detected. Changes in CO under the effect of hypoxia were individual (Fig. 2): increased, decreased, and unchanged CO were observed. Volume rate of cerebral blood flow during hypoxia increased ($p<0.005$; Table 1). No correlations between SV, CO changes, and increase in cerebral blood flow volume rate in the basins (vertebrobasilar basin, internal carotid artery basins) and common cerebral blood flow were detected.

The decrease in SV during inhalations of 8% hypoxic gas mixture was common for all volunteers; this decrease was in strong negative correla-

TABLE 1. Effect of Hypoxia on Central and Cerebral Hemodynamic Parameters

Parameter	Basal level	Hypoxia, min			Recovery, min			
		5	10	15	5	10	15	20
SpO_2, %	98±1	79±4***	73±5***	70±8***	71±12	96±4	98±1	98±1
HR, bpm	69±8	89±11***	91±12***	92±15***	64±9	67±10	71±9	72±8
Systolic AP, mm Hg	127±9	134±14	136±13	137±18	127±10	125±8	126±9	127±11
Diastolic AP, mm Hg	77±6	80±9	80±8	76±10	78±8	78±4	78±6	76±6
Volume rate of cerebral circulation, ml/100 g	48±9	62±14*	67±16**	71±22**	52±1	49±8	51±9	52±13
CO, liter	4.9±1.2	4.9±1.1	5.0±1.2	5.1±1.2	4.5±0.9	4.5±1.0	4.6±0.7	4.8±0.8

Note. *$p<0.005$, **$p<0.001$, ***$p<0.0001$ compared to basal level.

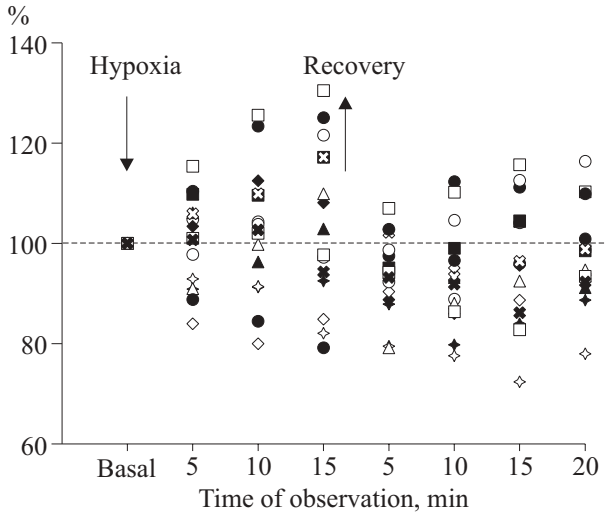

Fig. 2. Changes in cardiac output in volunteers. Ordinate: cardiac output (% of basal level).

tion with the increase in HR at the beginning of exposure and did not correlate with this parameter in the middle and at the end of exposure. Some authors explained the decrease in SV during hypoxia by impaired filling of heart ventricles because of high HR [1]. However, the increase in HR mainly shortens the diastole, while enhancement of sympathetic influences on the atria leads to more intensive blood ejection from the atria into ventricles, and ventricular filling virtually does not change even with HR increase to 150 bpm [2]. Our wavelet-based estimation of autonomic regulation of the heart rhythm showed that HR acceleration during the first minutes of hypoxia are primarily due to attenuation of the parasympathetic influences on the heart, while sympathetic influences manifests later. The decrease in SV at the beginning of exposure is due to HR increase because of really impossible ventricular filling during the first minutes. Later decrease in SV is due to the fact that hypoxia leading to constriction of many peripheral vessels (of the skin, gastrointestinal tract) reduces venous return and SV. We should like to emphasize that the obligatory decrease in SV during the transitional period and progress of hypoxia is an important compensatory mechanism allowing the heart provide blood supply under conditions of hypoxia, delaying exhaustion of the myocardium [6].

Individual reactions (in arbitrary units) of CO to hypoxia were revealed: from increase to decrease in the parameter. The use of traditional units (liter; Table 1) seemed to lead the authors to a conclusion about the absence of changes in CO during hypoxia. We did not intend to explain these differences in the present study, but it seems that they are due to peculiarities of metabolism in the volunteers. Presumably, the decrease or absence of changes in CO in the presence of subjective well-being is a sign of better compensation of acute hypoxia. The absence of correlation between CO changes and volumic rate of the cerebral blood flow seems to be a result of cerebral blood flow autoregulation.

Hence, exposure to acute hypoxic hypoxia, induced by inhalation of gas mixture with 8% oxygen in nitrogen, leads to reduction of SV in humans. This decrease is a result of not only increase in HR during the first minutes of exposure and subsequent peripheral vasoconstriction, but is also an important compensatory reaction of the cardiovascular system, preventing rapid energy exhaustion of the myocardium intensely working under conditions of hypoxia. Cardiac output can increase, decrease, or remain unchanged in different individuals, depending on their specific characteristics. Averaging of this parameter can give an illusion of its remaining unchanged during the study.

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