Impairment of Myocardial O₂ Supply due to Hyperventilation

By William A. Neill, M.D., and Mark Hattenhauer, M.D.

SUMMARY

Thirteen patients with ischemic coronary heart disease purposely hyperventilated for seven minutes in order to induce hypocapnic alkalosis. One patient experienced chest pain, and one exhibited chemical signs of myocardial hypoxia. Heart rate, blood pressure and myocardial O₂ consumption did not change significantly. Coronary blood flow decreased and coronary (a-v)O₂ difference widened. Since the alkalosis increased the blood O₂ affinity, the fall in Po₂ in coronary venous blood was proportionately even greater than the fall in O₂ concentration. Thus, hypocapnic alkalosis due to hyperventilation interferes with myocardial O₂ supply by 1) coronary vasoconstriction and 2) increased O₂ affinity of blood.

Hyperventilation increases arterial blood Po₂ and, by the Bohr effect, increases the affinity of blood for O₂ in proportion to the degree of hypocapnic alkalosis. The hemoglobin is more fully saturated with O₂ at any given Po₂, i.e., the O₂ dissociation curve is shifted to the left. Unless arterial hypoxemia was present initially, these changes only slightly augment oxygenation of arterial blood in the pulmonary capillaries, due to the configuration of the O₂ dissociation curve. At the same time, with the higher pH in the systemic capillaries, the hemoglobin will give up the expected amount of its O₂ only if the Po₂ falls below normal; and a decrease in capillary blood Po₂ might significantly impair O₂ diffusion into the tissue. In the coronary circulation where vasomotor regulation is influenced prominently by the needs of the myocardium for O₂, decreased capillary blood Po₂ might be expected to result in compensatory vasodilation and increased coronary blood flow, as in anemia. Hypocapnic alkalosis, however, increases vascular resistance and decreases blood flow in some tissues, including the forearm and brain. Although the results of experiments with the coronary circulation in anesthetized animals are inconclusive, voluntary hyperventilation has been reported to increase resistance, decrease blood flow and lower venous O₂ concentration in the normal coronary circulation of human subjects. Thus, in those subjects, the impaired blood O₂ release appeared not to be compensated by augmented blood flow but instead to be compounded by coronary vasoconstriction.

If increased blood O₂ affinity and coronary vasoconstriction also occur in patients with ischemic coronary heart disease, voluntary hyperventilation might result in myocardial hypoxia. The present report is an investigation of voluntary hyperventilation in the resting state in patients with symptomatic chronic ischemic coronary heart disease. We determined the effect of hyperventilation on systemic hemodynamics, coronary blood flow, myocardial O₂ supply, and in vivo O₂ affinity of coronary venous blood.

Methods

We studied 13 men with stable exertional angina pectoris who were being evaluated for possible coronary bypass graft surgery. Their ages ranged from 45 to 58 years (mean 50 years). Coronary arteriography was performed in 12 of the men and demonstrated single vessel disease in one patient, double vessel disease in five patients, and triple vessel disease in six patients. Four of the 11 patients with technically satisfactory left ventriculograms had ejection fractions < .50 or decreased regional wall motion. Eight patients had a previous myocardial infarction. No patient had significant valvular heart disease or clinical evidence of cardiac failure.

Written consent was obtained from the patients after we explained the investigative nature of the procedure. The patients practiced hyperventilating the day before the study. On the morning of the study, the patients fasted and received no sedation or nitrates. With the patient supine, we introduced catheters into the brachial artery percutaneously, coronary sinus via basilic vein cutdown, and into either the pulmonary artery via the same basilic vein cutdown or the left ventricle percutaneously via a femoral artery. Observations were made 1) with the patient at rest and 2) during the interval between the third and seventh minutes of vigorous, steady hyperventilation. The sequence was random. When hyperventilation was done first, we waited for 20–30 minutes before making resting observations.

ECG lead II and brachial artery and left ventricle pressures were recorded on a photographic Electronics for
MYOCARDIAL Oₐ SUPPLY IN HYPERVENTILATION

Medicine recorder. Paired arterial and coronary venous blood samples were analyzed for P₀₂ and pH (Radiometer Co., Copenhagen), hemoglobin concentration (spectrophotometer), and lactate and pyruvate concentrations. O₂ capacity of the blood was calculated from the hemoglobin concentration. Blood O₂ concentration or content (bound to hemoglobin and dissolved) was calculated from P₀₂ and O₂ capacity, after adjusting the O₂ dissociation curve for the observed pH change ("calculated" O₂ concentration values). Coronary venous blood O₂ concentration also was determined manometrically¹ in 11 patients ("manometric" O₂ concentration values). For coronary (a-v)O₂ difference we used calculated arterial O₂ concentration and manometric coronary venous O₂ concentration, except in the two patients in whom manometric analyses were not done. Coronary blood flow was determined in ten patients by the exponential clearance rate of ¹³³xenon.² The ¹³³xenon was injected via the left ventricle or pulmonary artery catheter, and the clearance rate was determined from timed coronary venous blood samples obtained through a manifold connected to the coronary sinus catheter. Five 15-second samples were withdrawn at a rate of 0.1 ml/sec during the early exponential clearance phase (between 30 and 105 seconds after injection, allowing for dead space in the sampling system). The clearance rate was corrected for arterial recirculation of ¹³³xenon. Left ventricle myocardial O₂ consumption was calculated as the product of coronary blood flow and coronary (a-v)O₂ difference. A lactate extraction coefficient, (a-v)/aL, less than 0.09, or an increase in coronary venous blood lactate/pyruvate concentration ratio (L/P) of greater than 12% (without accompanying increased arterial L/P) was interpreted as evidence of myocardial hypoxia.³

Results

Most patients experienced mild lightheadedness and tingling of the hands and lips, which began after 2 to 3 minutes and continued throughout the period of hyperventilation. In one patient, mild chest pain typical of his exertional angina occurred during the last two minutes of hyperventilation and subsided two minutes after normal breathing was resumed. No significant ST or T wave changes occurred in lead II of the ECG in any patient.

Hemodynamic data are summarized in table 1. There were no significant changes in heart rate, systemic arterial pressure or left ventricular end-diastolic pressure. Coronary blood flow decreased (fig. 1). Mean data for blood gases and pH are given in table 2. Hyperventilation decreased mean arterial blood Pco₂ to 18.7 mm Hg and increased mean arterial blood pH to 7.56. Arterial blood P₀₂ and O₂ concentration increased (fig. 2). Coronary venous blood P₀₂ and O₂ concentration both decreased (figs. 3 and 4), but P₀₂ decreased by a proportionately greater amount. This discrepancy can be explained by the coronary venous blood alkalosis since mean coronary venous blood O₂ concentration calculated from the P₀₂ and pH values was not significantly different from O₂ concentration determined by manometric analysis (calculated value was greater by a mean of 0.3 ml/100 ml). Thus, hyperventilation exerted no significant effect on blood O₂ affinity other than that attributable to the increase in pH.

The fall in coronary blood flow was accompanied by a proportional widening of the coronary (a-v)O₂, and there was no significant change in myocardial O₂ consumption.

Lactate and pyruvate data are given in table 3. The arterial blood lactate concentration increased during hyperventilation. Extraction of pyruvate by the myocardium decreased significantly, whereas the

| Table 1 | Hemodynamic Data
<table>
<thead>
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<tbody>
<tr>
<td></td>
<td>Rest</td>
</tr>
<tr>
<td>HR (min⁻¹)</td>
<td>71 ± 2.2*</td>
</tr>
<tr>
<td>SAPs (mm Hg)</td>
<td>140 ± 3.6</td>
</tr>
<tr>
<td>SAPd (mm Hg)</td>
<td>72 ± 2.7</td>
</tr>
<tr>
<td>SAPm (mm Hg)</td>
<td>100 ± 2.8</td>
</tr>
<tr>
<td>LVEDP (mm Hg)</td>
<td>14 ± 2.3</td>
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<tr>
<td>CBF (ml/100 g · min)</td>
<td>99 ± 6.7</td>
</tr>
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</table>

*Mean = SEM.
†Seven patients.
‡Statistical difference, hyperventilation vs rest (paired t-test), P < 0.05.

Abbreviations: HR = heart rate; SAP = systemic arterial blood pressure; s = systole; d = diastole; m = mean; LVEDP = left ventricular end-diastolic blood pressure; CBF = coronary blood flow.

Figure 1

Effect of four minutes of voluntary hyperventilation on coronary blood flow (¹³³Xe). Each line represents one patient. Mean values for coronary blood flow at rest and during hyperventilation are indicated.
Discussion

These studies show that hyperventilation decreased coronary blood flow and coronary venous blood $O_2$ concentration in patients whose myocardial $O_2$ supply was already compromised by ischemic coronary disease. Since systemic arterial blood pressure did not change significantly during hyperventilation, the observed decrease in coronary blood flow implies increased coronary resistance. Coronary vascular resistance normally is responsive to simultaneous changes in myocardial $O_2$ needs, so that coronary (a-v)$O_2$ difference remains nearly constant. In our studies, however, no fall in myocardial $O_2$ needs occurred. Heart rate and systolic arterial blood pressure, important determinants of myocardial $O_2$ needs, did not decrease; and calculated myocardial $O_2$ consumption remained essentially constant. Moreover, the widening of the coronary (a-v)$O_2$ difference is inconsistent with decrease in $O_2$ needs as the basis of the decrease in blood flow. When arterial blood $O_2$ concentration was augmented by breathing high concentrations of $O_2$, coronary blood flow decreased.12,13 Under those circumstances, however, coronary venous blood $O_2$ concentration rises,12-15 and the decrease in coronary blood flow presumably is due to a reduction in the amount of blood flow needed to maintain myocardial $O_2$ supply. The slight increase in arterial blood $O_2$ concentration which occurred during hyperventilation in our patients, however, cannot explain their decrease in blood flow, since their coronary

![Figure 2](image1)

**Figure 2**
*Effect of five minutes of voluntary hyperventilation on arterial blood $O_2$ concentration.*

A slight decrease in lactate extraction was not statistically significant. One patient developed a significant (20%) increase in coronary venous blood L/P, indicative of myocardial hypoxia (Methods). None developed an abnormally low lactate extraction.

![Figure 3](image2)

**Figure 3**
*Effect of five minutes of voluntary hyperventilation on coronary venous blood $O_2$ concentration.*

![Figure 4](image3)

**Figure 4**
*Effect of five minutes of voluntary hyperventilation on coronary venous blood $Po_2$.*
Table 2

<table>
<thead>
<tr>
<th>Blood Gas Data</th>
<th>Rest</th>
<th>Hyperventilation</th>
</tr>
</thead>
<tbody>
<tr>
<td>P_{CO_2} (mm Hg)</td>
<td>33.1 ± 1.22*</td>
<td>18.7 ± .74***</td>
</tr>
<tr>
<td>pHa (units)</td>
<td>7.40 ± .007</td>
<td>7.56 ± .009***</td>
</tr>
<tr>
<td>pHv (units)</td>
<td>7.36 ± .008</td>
<td>7.50 ± .010***</td>
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<tr>
<td>P_{O_2a} (mm Hg)</td>
<td>66 ± 2.2</td>
<td>84 ± 3.7***</td>
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<tr>
<td>P_{O_2v} (mm Hg)</td>
<td>19.5 ± .67</td>
<td>16.3 ± .56***</td>
</tr>
<tr>
<td>O_{2} Cap (ml/100 ml)</td>
<td>20.4 ± .62</td>
<td>20.5 ± .62***</td>
</tr>
<tr>
<td>C_o2 (ml/100 ml)</td>
<td>19.1 ± .53</td>
<td>20.2 ± .61***</td>
</tr>
<tr>
<td>C_{v-o2} (ml/100 ml)</td>
<td>6.1 ± .20</td>
<td>5.5 ± .24***</td>
</tr>
<tr>
<td>C(a-v)O_{2} (ml/100 ml)</td>
<td>13.0 ± .50</td>
<td>14.7 ± .59***</td>
</tr>
<tr>
<td>MVO_{2} (ml/100 g · min)</td>
<td>12.7 ± .88</td>
<td>12.8 ± .76</td>
</tr>
</tbody>
</table>

*Mean ± SEM.
**P < 0.01, hyperventilation vs rest, paired t-test.
***P < 0.001, hyperventilation vs rest, paired t-test.

Ten patients.

Abbreviations: P = partial pressure; a = arterial; v = venous coronary; Cap = capacity; MVO_{2} = myocardial O_{2} consumption.

Venous blood O_{2} concentration decreased. The decrease in coronary blood flow appears to be due to a direct vasoconstrictive effect of the hyperventilatory alkalosis. Our data do not distinguish between hypocapnia and alkalosis as potential causes of the coronary vasoconstriction. Other experiments, however, suggest that alkalosis is more likely responsible for the vasoconstriction.5, 10-18

Hyperventilation raised arterial blood O_{2} concentration by 5%, which represents a minor potential benefit to myocardial O_{2} supply. By contrast, the simultaneous detrimental effect of increased O_{2} affinity of the blood on its ability to release O_{2} in the coronary capillaries was quantitatively much more powerful. In a previous investigation in humans,6 coronary venous blood P_{O_2} was calculated from O_{2} concentration, assuming that the increase in pH was the only factor influencing blood O_{2} affinity. In the present study, changes in blood O_{2} affinity can be examined directly in the 11 patients in whom coronary venous blood P_{O_2} and O_{2} concentration were both measured. In these 11 patients, mean coronary venous blood O_{2} concentration fell from 6.2 to 5.6 ml/100 ml. If blood O_{2} affinity were to remain constant, that fall in O_{2} concentration would correspond to a decrease in P_{O_2} only from 19.5 to 18.5 mm Hg. Yet, coronary venous blood P_{O_2} fell to 16.2 mm Hg. Conversely, with a constant O_{2} affinity, the observed decrease in P_{O_2} to 16.2 mm Hg would have permitted a fall in coronary venous blood O_{2} concentration to as low as 4.4 ml/100 ml, widening the coronary (a-v)O_{2} difference and augmenting myocardial O_{2} delivery by 8%. These data constitute direct evidence for increased blood O_{2} affinity and decreased O_{2} release in the coronary capillaries. The increase found in O_{2} affinity was approximately equal to that predicted by the blood pH change which occurred.

These experiments demonstrate that hyperventilatory alkalosis interferes with myocardial O_{2} supply by a combination of coronary vasoconstriction and increased O_{2} affinity of the blood in the coronary capillaries. This effect of hyperventilation could be important in several clinical situations. 1) Pulmonary vascular congestion. The hyperventilatory alkalosis that frequently results from dyspnea could potentiate myocardial hypoxia and further impair left ventricular function. 2) Angina pectoris provoked by cold or emotion. The sensitivity of certain patients with ischemic heart disease to cold exposure or emotional stress might be due to associated hyperventilation.10 3) Psychoneurotic chest pain. Chronic hyperventilation frequently occurs in anxiety without being apparent to either the patient or the observer.19 Even when initiated voluntarily, when hyperventilation is maintained, the sensation of excessive breathing may largely recede within an hour while asymptomatic hyperventilatory alkalosis remains as severe as in our patients.20 4) Exertional chest pain and ST-segment depression despite normal coronary angiograms.21-23 Some observers have been impressed by the prevalence of anxiety in these patients. Excessive breathing during exercise is an unexplored possible basis of their manifestations of exertional myocardial hypoxia.

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