Effects of Respiratory Alkalosis on Oxygen Consumption and Oxygenation

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The effect of respiratory alkalosis on oxygen consumption after passive hyperventilation was studied in eight dogs. Pa_{CO_2} decreased from 32.1 to 13.6 torr, pH increased from 7.43 to 7.72, and oxygen consumption increased from 116.5 to 147.5 ml/m²/min. Venous admixture decreased from 17.1 to 8.8 per cent during passive hyperventilation, while cardiac index, Pa_{O_2}, Sa_{O_2} and Ca_{O_2} did not change significantly. Using a model, it can be shown that if oxygen consumption did not increase, Pa_{O_2}, Sa_{O_2} and Ca_{O_2} during hyperventilation would be higher than the values observed experimentally. The observed increase in $\dot{V}_{O_2}$ during respiratory alkalosis prevents a maximal increase in arterial oxygenation in the normal animal. (Key words: Hyperventilation; Alkalosis; Oxygen consumption; Oxygenation.)

ARTERIAL OXYGENATION during anesthesia can be altered by several factors. When blood oxygen capacity is constant, arterial blood oxygen content (Ca_{O_2}) is determined by pulmonary end-capillary oxygen content (Cc'_{O_2}), right-to-left shunt ($\dot{Q}s/\dot{Q}_T$)[1] (or venous admixture $\dot{Q}_{VA}/\dot{Q}_T$,[2] depending on mixed oxygen concentration), cardiac output ($\dot{Q}_T$)[3,4] and oxygen consumption ($\dot{V}_{O_2}$). One factor receiving little attention is the effect of an increased $\dot{V}_{O_2}$ of the body. Alkalosis accompanying passive hyperventilation has been reported[5] to increase $\dot{V}_{O_2}$ significantly. This increase in $\dot{V}_{O_2}$, resulting from respiratory alkalosis, represents a new and important factor in altering arterial oxygenation. During breathing of air, hyperventilation is expected to improve arterial oxygenation. The purpose of this study was to determine the extent to which the increased $\dot{V}_{O_2}$ modifies the increase

in arterial oxygenation seen during hyperventilation with air.

Methods

Eight dogs with an average weight of 10.6 kg were anesthetized with pentobarbital, 30 mg/kg, given intravenously; anesthesia was then maintained with a continuous infusion of pentobarbital, 0.2 mg/kg/min. The trachea was intubated with a large-bore endotracheal tube and the cuff inflated to give an airtight fit. Dogs were initially ventilated with air ($F_{I_{O_2}} = 0.209$), using a constant-volume respirator for a control period of one hour, then hyperventilated for two hours, increasing both tidal volume (V_T) and respiratory frequency (f) in one step from 0.48 to 0.84 l/m² and 14 to 28/min, respectively (average values). A third period using the initial minute volume lasted two additional hours. Temperature was measured by a thermistor placed in the lower third of the esophagus and maintained at 37 ± 0.5 C with a thermal blanket.

Arterial blood samples were obtained from a catheter placed in the femoral artery. Mixed venous blood samples were obtained from a catheter placed in the pulmonary artery via an external jugular vein. Location of the catheter was confirmed by pulse–pressure contour.[6] Blood samples were collected anaerobically in heparinized glass syringes and iced immediately. An Instrumentation Laboratory, Inc. (Boston, Mass.) Model 313 blood–gas analyzer was used to measure arterial and mixed venous oxygen (Pa_{O_2}, $P\bar{v}_{O_2}$) and carbon dioxide (Pa_{CO_2}, $P\bar{v}_{CO_2}$) tensions and pH (pH_a, pH_v). Corrections were made for loss of oxygen in the iced sample during the interval before analysis[7] and for O_2 electrode blood–gas difference by tonometry.[8] Using the Rossing and Cain nomogram,[9] oxyhemoglobin saturation was determined from the measured blood P_{O_2} and pH. Blood oxygen content in vol per cent was calculated using 1.38 ml O_2/g

TABLE 1. Effects of Hyperventilation on Pulmonary Gas Exchange*

	I Control 1 Hour	II Hyperventilation 2 Hours	III Recovery 2 Hours
pH$_a$	7.43±0.03	7.72±0.08‡	7.41±0.02
Pa$_{CO_2}$, torr	32.1 ±2.2	13.6 ±1.0‡	30.5 ±2.3
Pa$_{O_2}$, torr	86.8 ±5.0	90.7 ±7.3	91.1 ±4.3
Sa$_{O_2}$, per cent	95.0 ±0.7	98.1 ±0.2‡	95.6 ±0.6
Ca$_{O_2}$, vol per cent	17.4 ±0.5	18.6 ±0.5	17.0 ±0.5
V̇$_{E\,BTPS}$ l/m² min	6.70±0.52	23.71±1.08‡	6.72±0.52
V̇$_{CO_2\,STPD}$ ml/m² min	100.7 ±5.5	119.0 ±5.7‡	94.7 ±5.8
V̇$_{O_2\,STPD}$ ml/m² min	116.5 ±5.2	147.5 ±10.6‡	115.0 ±6.1
R	0.87±0.3	0.82±0.04	0.83±0.01
V$_D$/V$_T$ per cent	47.0 ±1	61.0 ±3‡	46.0 ±2
Q̇$_{VA}$/Q̇$_T$ per cent	17.1 ±3.2	8.8 ±1.2†	8.1 ±1.9‡
CI l/m²/min	4.9 ±0.5	4.4 ±0.7	2.8±0.4¶
Ca$_{O_2}$ − C$\bar{v}_{O_2}$ vol %	2.38±0.24	3.35±0.42‡	4.1 ±0.49‡

* Values are means ±SE. Paired t test was used to compare hyperventilation with control (II *vs.* I) and recovery with control (III *vs.* I).
† $P < 0.05$;　‡ $P < 0.01$;　¶ $P < 0.002$;　‡ $P < 0.001$.

hemoglobin when fully saturated plus 0.003 ml dissolved O_2/torr P_{O_2}/100 ml blood.

Expired minute ventilation (V̇$_E$) was measured on a Collins 13.5-liter spirometer. V̇$_{O_2}$, CO_2 production (V̇$_{CO_2}$), and respiratory quotient (R) were derived from analysis of mixed expired air using an open-circuit technique. Expired gas samples were collected at the end of each period in aluminum-lined gas-collection bags for measurement of mixed expired oxygen ($F_{E_{O_2}}$) and carbon dioxide ($F_{E_{CO_2}}$) concentrations, using the Scholander analyzer.[10]

Venous admixture (Q̇$_{VA}$/Q̇$_T$) was calculated from the following:

$$\frac{\dot{Q}_{VA}}{\dot{Q}_T} = \frac{Cc'_{O_2} - Ca_{O_2}}{Cc'_{O_2} - C\bar{v}_{O_2}}$$

where Cc'_{O_2}, Ca_{O_2} and $C\bar{v}_{O_2}$ represent end-capillary, arterial, and mixed venous blood oxygen contents, respectively. Alveolar oxygen tension ($P_{A_{O_2}}$) is assumed equal to end-capillary oxygen tension (Pc'_{O_2}). Cardiac index (CI) was calculated using the Fick principle. Dead-space-to-tidal volume ratio (V$_D$/V$_T$) was calculated assuming alveolar CO_2 tension ($P_{A_{CO_2}}$) is equal to Pa$_{CO_2}$.

Results

Average values are summarized in table 1. During two hours of hyperventilation Pa$_{CO_2}$ decreased from 32.1 ± 2.2 to 13.6 ± 1.0 torr ($P < 0.001$) and pH_a increased from 7.43 ± 0.03 to 7.72 ± 0.08 ($P < 0.001$). During this period V̇$_{O_2}$ increased from 116.5 ± 5.2 to 147.5 ± 10.6 ml$_{STPD}$/m²/min ($P < 0.01$), an increase of 25 per cent. Following two hours of recovery, the above values closely approximated those obtained during the control period. The values of Pa$_{O_2}$ and Ca$_{O_2}$ during the control and hyperventilation periods increased from 86.8 ± 5.0 to 90.7 ± 7.3 torr and 17.4 ± 0.4 to 18.6 ± 0.5 vol per cent, respectively, but were not statistically significant. Q̇$_{VA}$/Q̇$_T$ decreased from 17.1 ± 3.2 to 8.8 ± 1.2 per cent ($P < 0.05$) during hyperventilation, but changed little during recovery. During hyperventilation CI decreased from 4.9 ± 0.5 to 4.4 ± 0.7 l/m²/min (not a significant change), but during the recovery period CI decreased significantly to 2.8 ± 0.4 l/m²/min ($P < 0.02$).

Discussion

The present study has demonstrated that when pH_a is increased from 7.43 to 7.72 by passive hyperventilation there is an increase in V̇$_{O_2}$ from 116.5 to 147.5 ml$_{STPD}$/m²/min, an increase of 25 per cent. In 1958, Huckabee[11] reported that with a threefold increase of mechanical ventilation in dogs there is an increase in V̇$_{O_2}$ of 10 per cent. Nahas and Poyart[12] made a similar observation in dogs during hyperventilation. Cain[5] showed that hyperventilation alkalosis produced in one or several steps resulted in increased V̇$_{O_2}$. Further studies by Karetzky and Cain[13,14] demonstrated that the increased V̇$_{O_2}$ seen during hyperventilation was reversed by an infusion of HCl or adding CO_2 to the inspired air. The increase in V̇$_{O_2}$ is dependent upon the decrease in [H$^+$] and not on the low P_{CO_2} as such. In the present study, as in the previous studies,[5] a significant correlation between pH_a and V̇$_{O_2}$ was demonstrated:

$$\dot{V}_{O_2}(ml/m²/min) = -733.9 + [pH_a \cdot (114.7)],$$
$$r = 0.65 \ (P < 0.002)$$

The mechanism by which alkalosis increases $\dot{V}_{O_2}$ remains uncertain. Tenny and Lamb[15] have suggested that alkalosis produces mitochondrial swelling, which implies increased $\dot{V}_{O_2}$. It has been shown that with alkalosis there is increased lactate production[16, 17] reflecting increased glycolysis. Phosphofructokinase, a "key" enzyme in the glycolytic cycle, which has its activity greatly increased by an alkaline pH,[18, 19] may be proven responsible for the increased $\dot{V}_{O_2}$. The effects of acidosis and increased $[H^+]$ on $\dot{V}_{O_2}$, although not studied here, are expected to decrease $\dot{V}_{O_2}$.[5, 12]

Hyperventilation is expected to increase physiologic deadspace, and this was observed in this study. In a computer model of pulmonary gas exchange, West has shown that with a constant distribution of pulmonary ventilation–perfusion ratios $(\dot{V}_A/\dot{Q}_c)$, an increase in ventilation increases V_D/V_T and reduces $\dot{Q}_{VA}/\dot{Q}_T$.[20] In the present study, V_D/V_T increased significantly from 47 to 61 per cent during hyperventilation. $\dot{Q}_{VA}/\dot{Q}_T$ decreased significantly during hyperventilation, from 17.1 to 8.8 per cent. Following return of ventilation to its initial value, V_D/V_T decreased as expected; however, $\dot{Q}_{VA}/\dot{Q}_T$ did not increase significantly, implying that the improvement in the distribution of $\dot{V}_A/\dot{Q}_c$ is not easily reversible.

Mechanical ventilation with sustained elevation of airway pressure (not used here) impedes venous return and decreases cardiac output $(\dot{Q}_T)$.[21] In the present study, end-expiratory pressure was zero, and there was no significant change in $\dot{Q}_T$ during hyperventilation, CI being 4.4 $l/m^2/min$ compared with 4.9 $l/m^2/min$ during the control period. However, during the recovery period CI decreased to 2.8 $l/m^2/min$ $(P < 0.001)$. This decrease could be explained on the basis of prolonged anesthesia. It has been shown in dogs that following an initial dose of pentobarbital after 4 hours of mechanical ventilation, there is a 25 per cent decrease in $\dot{Q}_T$[22]; when the animals received a supplementary dose of pentobarbital every hour, the decrease was 45 per cent.[23] In the present study the pentobarbital infusion rate remained constant. During the recovery period following hyperventilation, $\dot{V}_{O_2}$ returned to the control level, indicating that the level of narcosis had not deepened. The reason for the
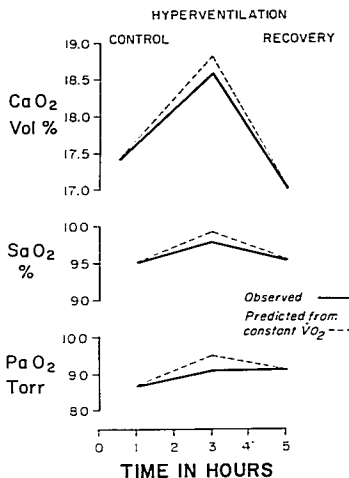

FIG. 1. Arterial blood oxygen values during hyperventilation. Solid lines represent values obtained experimentally. Dotted lines represent changes predicted during hyperventilation when $\dot{V}_{O_2}$ does not increase above the control value.

decrease in CI during the recovery from hyperventilation is unknown.

One of the central issues here is the effect of increased $\dot{V}_{O_2}$ on arterial oxygenation. When blood oxygen on capacity is constant, Ca_{O_2} is affected by changes in Cc'_{O_2}, $\dot{Q}_{VA}/\dot{Q}_T$, $\dot{Q}_T$, and $\dot{V}_{O_2}$, as shown in the following equation:

$$Ca_{O_2} = Cc'_{O_2} - \left[\frac{\dot{Q}_{VA}}{\dot{Q}_T} \cdot \frac{\dot{V}_{O_2}}{(\dot{Q}_T - \dot{Q}_{VA})} \right]$$

Thus, it can be seen that an increase in $\dot{Q}_{VA}/\dot{Q}_T$, or an increase in $\dot{V}_{O_2}$, or a decrease in $\dot{Q}_T$ will lead to a decrease in Ca_{O_2}. In the present study Ca_{O_2} increased from 17.4 to 18.6 vol per cent during hyperventilation. The value of Ca_{O_2} is the result of opposing factors described above. For example, the decrease in CI from period II to period III is counterbalanced by the decrease in $\dot{V}_{O_2}$, resulting in a negligible change in Pa_{O_2}. Although it is not possible to maintain $\dot{Q}_{VA}/\dot{Q}_T$ constant during hyperventilation, nevertheless it is possible to evaluate the effect of increased $\dot{V}_{O_2}$. To demon

strate this, we first plot the experimentally obtained values of Pa_{O_2}, Sa_{O_2} and Ca_{O_2} (fig. 1). Now, if $\dot{V}_{O_2}$ did not increase during hyperventilation, then in each instance the predicted values (represented by the dotted lines) would be higher than those actually observed during the study. The higher values would be Pa_{O_2} from 90.7 to 95 torr, Sa_{O_2} from 98.1 to 99.2 per cent, and Ca_{O_2} from 18.6 to 18.8 vol per cent, thus showing that in a normal anesthetized dog increased oxygen consumption prevented or attenuated the expected change in arterial oxygenation.

The important consideration here is to recognize that these changes, although minimal in an otherwise-normal subject, become more important in cardiopulmonary disease.

During general anesthesia a major contributor to hypoxemia is an increased $\dot{Q}_S/\dot{Q}_T$. Two examples of the effect of increased $\dot{V}_{O_2}$ on arterial oxygenation derived from a model follow. First, assume that in an anesthetized subject (fig. 2) $F_{I_{O_2}} = 0.40$, $Hb = 15\,g/100\,ml$,

$R = 0.8$, $CI = 3\ l/m^2/min$, and base excess $= 0$. When all these factors remain constant and the only changes are a decrease in Pa_{CO_2} and an increase in pH_a associated with hyperventilation, then the relationships seen in figure 2 will hold. $\dot{V}_{O_2}$ of 130 ml/m²/min represents a basal value. The increase in $\dot{V}_{O_2}$ is predicted from the changes in human subjects reported by Karetzky and Cain,[12] and is also consistent with the data in the present study. On the left vertical axis, Cc'_{O_2} and Ca_{O_2} are represented. On the right vertical axis, for purposes of comparison, are the equivalent Sa_{O_2} and Pa_{O_2} for the oxygen dissociation curve at a pH_a of 7.40. Represented on the center portion are the values of Ca_{O_2} with $\dot{Q}_S/\dot{Q}_T$ ranging from 20 to 50 per cent. We find that although the Cc'_{O_2} increases with the increase in Pa_{O_2} associated with hyperventilation, the increased $\dot{V}_{O_2}$ as a result of this hyperventilation, together with a constant fraction of $\dot{Q}_T$ present as $\dot{Q}_S/\dot{Q}_T$, results in a decrease in Ca_{O_2}, and that this effect is magnified with an increasing
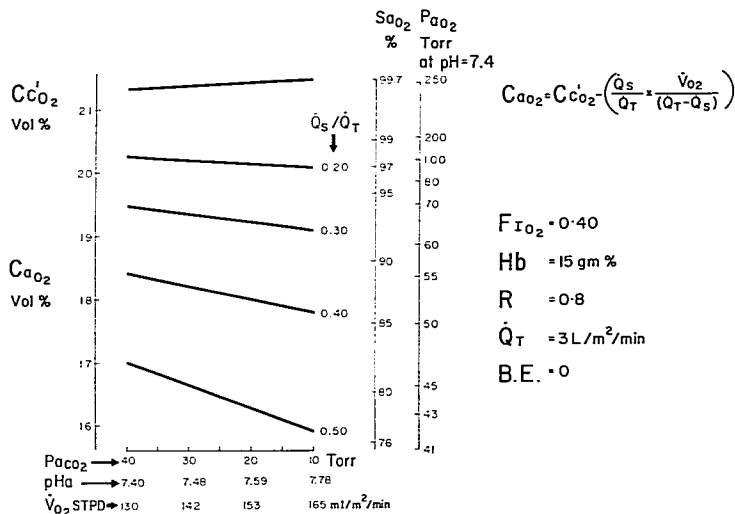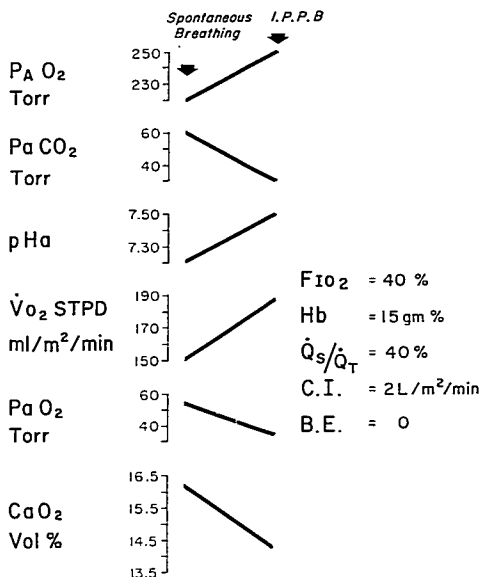

FIG. 2. A model: the magnitudes of decreases in Ca_{O_2} with increasing $\dot{V}_{O_2}$ from respiratory alkalosis at different values of $Q_S/\dot{Q}_T$. Equivalent values of P_{O_2} and S_{O_2} are given for comparison.

FIG. 3. A model: the effect of hyperventilation in an ill patient with respiratory acidosis and low fixed cardiac output.

$\dot{Q}_S/\dot{Q}_T$. An example seen in clinical practice is patients with various degrees of intracardiac shunts.

Now (fig. 3), take an ill patient who is breathing 40 per cent O_2, has a normal Hb of 15 g/100 ml, a high $\dot{Q}_S/\dot{Q}_T$ of 40 per cent, a low fixed CI of 2 l/m²/min, and no metabolic acidosis, base excess = 0; this patient while breathing spontaneously has a $\dot{V}_{O_2}$ of 150 ml/m²/min, respiratory acidosis, Pa_{CO_2} 60 torr, pH 7.2, and Pa_{O_2} 53 torr. It would be common practice to put this patient on a ventilator, reversing the respiratory acidosis, and for the purposes of this illustration, lowering Pa_{CO_2} from 60 to 30 torr. This would increase pH from 7.2 to 7.5 and, if the change in $\dot{V}_{O_2}$ is predictable, it would increase oxygen consumption to 187.5 ml/m²/min. With no change in $\dot{Q}_S/\dot{Q}_T$ or $\dot{Q}_T$ there would be a reduction in oxygen content of arterial blood and Pa_{O_2} would decrease from 53 to 35 torr in spite of an actual increase in Pa_{O_2} associated with the hyperventilation. In each of the model cal-

culations above, base excess is taken as zero in order to point out the direct relation of respiratory alkalosis to increased $\dot{V}_{O_2}$. It is well known that the patient with arterial hypoxemia is expected to have some metabolic acidosis, which, in turn, may attenuate the alkalotic effect of hyperventilation.

We conclude that in the presence of venous admixture or shunting the increased oxygen consumption of the body associated with respiratory alkalosis will alter arterial oxygenation. This effect has important implications in patient management and represents a potential hazard when using hyperventilation.

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Obstetrics

ANESTHESIA EFFECT ON LABOR The second stage of labor was studied in 42 patients before and after conduction anesthesia. Intrauterine pressure and superimposed voluntary effort before and after induction of anesthesia were measured and compared. Voluntary effort increased progressively during the second stage in patients receiving pudendal block. Patients having peridural block showed a slight decrease in voluntary effort. Patients with spinal block had a mean reduction in voluntary effort after the block. Patients receiving peridural block showed a mean decrease in the intensity of uterine contractions, but no change in contraction intensity was seen after pudendal or spinal block. A review of the records of 3,265 primigravid term patients revealed an increased length of the second stage and an increased incidence of forceps deliveries in patients with spinal and peridural anesthesia compared with pudendal anesthesia. (*Johnson, W. L., and others: Effect of Pudendal, Spinal, and Peridural Block Anesthesia on the Second Stage of Labor, Am. J. Obstet. Gynecol. 113: 166–175, 1972.*)