Effect of α-Stat Versus pH-Stat Strategy on Oxyhemoglobin Dissociation and Whole-Body Oxygen Consumption During Hypothermic Cardiopulmonary Bypass

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To determine whether α-stat or pH-stat strategy should be used, 20 patients undergoing coronary artery bypass grafting during moderate hypothermic hemodilutional cardiopulmonary bypass were studied. The carbon dioxide management during bypass was randomly done according to α-stat strategy in 10 patients (i.e., temperature-uncorrected Paco₂ was kept near 40 mm Hg and uncorrected pH was kept at about 7.4) and according to pH-stat strategy in the other 10 patients (i.e., temperature-corrected Paco₂ was kept near 40 mm Hg and uncorrected pH was kept at about 7.4). In both groups, when the central venous temperature was stable at 26.5 °C, the perfusion flow was altered sequentially from 2.4 to 1.8 and 1.2 L.min⁻¹.m⁻². The mixed venous oxyhemoglobin saturation at the different perfusion flows was monitored by the Oxy-Stat meter and was correlated with the corresponding mixed venous oxygen tension to construct an oxyhemoglobin dissociation curve. Also, the whole-body oxygen consumption at the different perfusion flows was computed. The whole-body oxygen consumption and the oxyhemoglobin dissociation were not significantly different between the α-stat and the pH-stat groups. In both groups, the dissociation curve is shifted to the left, but the oxygen consumption per unit time does not significantly change despite decreasing the perfusion flow from 2.4 to 1.2 L.min⁻¹.m⁻². The results suggest that oxygen delivery is not impaired during moderate hypothermic cardiopulmonary bypass independent of whether α-stat or pH-stat strategy is used.

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The strategy of acid-base management during hypothermic cardiopulmonary bypass (CPB) has been a controversial issue (1-3). Two main strategies of acid-base management may be followed during hypothermic CPB: pH-stat, whereby a temperature-corrected Paco₂ of near 40 mm Hg and corrected pH near 7.4 are maintained at the different body temperatures; and α-stat whereby the temperature-uncorrected Paco₂ (measured at 37°C) is kept near 40 mm Hg and the uncorrected pH is kept near 7.4, irrespective of the body temperature (2,3).

Hypothermia shifts the oxyhemoglobin dissociation curve to the left (4). The leftward shift may be exaggerated by the relative alkalosis that characterizes the α-stat strategy of acid-base regulation (5). Thus, hypothermia and alkalosis may be a double hazard that reduces the available oxygen (6). In contrast with α-stat, the pH-stat strategy of acid-base regulation maintains the temperature-corrected pH and Paco₂ during hypothermia at the normothermic values and hence may be used to counter the leftward shift of the oxyhemoglobin dissociation curve engendered by hypothermia (3).

The present report compares the effect of pH-stat versus α-stat management on the oxyhemoglobin dissociation in two groups of patients undergoing coronary artery bypass grafting during moderate hypothermic CPB. In the two groups, the perfusion flow was altered to achieve a spectrum of mixed venous oxyhemoglobin saturation (SVO₂) and mixed venous oxygen tension (PVo₂) values that can be correlated. Also, the whole-body oxygen consumption (VO₂) values at the different perfusion flows were compared.

Methods

The investigation was performed on 20 patients, aged 40-75 yr and weighing 60-90 kg, who were undergoing coronary artery bypass grafting. The patients...
were randomized with respect to carbon dioxide management during CPB into two groups. In 10 patients, the temperature-uncorrected $\mathrm{Paco}_2$ was maintained at about 40 mm Hg ($\alpha$-stat), whereas the temperature-corrected $\mathrm{Paco}_2$ was maintained at this range in the other 10 patients (pH-stat). The investigation was approved by the Institution Research Committee, and informed consent was obtained.

All patients were premedicated with 10 mg of morphine, 25 mg of promethazine, and 0.4 mg of scopolamine, intramuscularly. Anesthesia was induced with 0.1 mg/kg of midazolam, 50 $\mu$g/kg of fentanyl, and a mixture of 0.1 mg/kg of vecuronium and 0.1 mg/kg of pancuronium IV. After orotracheal intubation, ventilation was controlled with 100% oxygen, without any inhaled anesthetic supplementation. Patients were monitored with an electrocardiogram (V3), a radial artery catheter, and a pulmonary artery catheter.

Before CPB, the patients were given lactated Ringer's solution at a rate of 10 mL/kg, and an additional 1500 mL was used to prime the Bentley bubble oxygenator (Bentley-10, American Bentley). No blood or colloid was added to the prime. During bypass, the mean hematocrit level was 23.9% $\pm$ 3.5% in the $\alpha$-stat group and 24.1% $\pm$ 2.9% in the pH-stat group. The patients were perfused by a roller pump (Sarns 5000, Ann Arbor, Mich.) at a flow rate of 2.4 L·min$^{-1}$·m$^{-2}$, and the flow was monitored by a flow rate computer (Sarns). In the $\alpha$-stat group of patients, an equal flow of 100% oxygen without any additional carbon dioxide was continuously delivered to the bubble oxygenator during hypothermia and after rewarsembling (7). In the pH-stat group, carbon dioxide was added to the oxygen flow delivered to the oxygenator and was adjusted according to blood gas results to maintain the temperature-corrected $\mathrm{Paco}_2$ at around 40 mm Hg.

Continuous in-line oximetry of the venous saturation was achieved by the Oxy-Stat meter (8,9). The Oxy-Stat meter has shown accuracy and reliability during extracorporeal circulation, as evidenced by the excellent correlation between the oxyhemoglobin saturation measured by the Oxy-Stat meter and that determined by the van Slyke and Lex O$_2$ con (10). The site for body temperature and $\mathrm{SvO}_2$ monitoring, as well as mixed venous gas sampling, was the venous blood at the entrance to the pump oxygenator (11), whereas arterial blood was sampled simultaneously from the outlet of the oxygenator. Blood gas levels were measured by an ABL300 Radiometer with electrodes kept constant at 37°C. The temperature-uncorrected values measured at 37°C were then corrected automatically by the radiometer according to body temperature. In the ABL300 blood gas analyzer, correction is done by using formulas based on work by Severinghaus (12) for pH, by Siggard-Anderson (13) for $\mathrm{PCO}_2$ and by Severinghaus et al. (14) for $\mathrm{PO}_2$.

During CPB, body temperature was decreased, and the heart was arrested after aortic cross-clamping with a cardiopulmonary solution (K+, 30 mEq/L at 4°C). After 10-20 min of CPB, a steady state of perfusion was achieved and the mean body temperature was stabilized at 26.5 $\pm$ 2.5°C. In both the $\alpha$-stat and the pH-stat groups, the $\mathrm{SVo}_2$ as well as the mixed venous and arterial blood gases were monitored simultaneously when the perfusion flow was maintained at 2.4 L·min$^{-1}$·m$^{-2}$. The perfusion flow was then decreased in sequence to 1.8 and 1.2 L·min$^{-1}$·m$^{-2}$. The resulting $\mathrm{SVo}_2$ and blood gas values were recorded 5 min after each perfusion flow change. The $\mathrm{SVo}_2$ values achieved at the different perfusion flows were correlated with the corresponding temperature-corrected $\mathrm{PVO}_2$ values in the two groups of patients to construct oxyhemoglobin dissociation curves.

The $\mathrm{VO}_2$ values at the different perfusion flows were computed as the product of the arterial-venous oxygen content difference multiplied by the perfusion flow:

$$\mathrm{VO}_2 \text{(mL·min}^{-1} \cdot \text{m}^{-2}) = \frac{[(\mathrm{Sao}_2 \% - \mathrm{SVo}_2 \%)}{\times \mathrm{Hb}} \times 1.361 \times \frac{\mathrm{CI}}{1.36}$$

where $\mathrm{CI}$ = perfusion flow index (dL·min$^{-1}$·m$^{-2}$); $\mathrm{Sao}_2 \% = \text{mixed venous oxygen saturation}$, measured by the Bentley oximeter; $\mathrm{Hb} = \text{hemoglobin concentration (g/dL)}$, calculated as hematocrit /3; 1.36 = Haffner factor; $\mathrm{Pao}_2 = \text{uncorrected arterial oxygen tension (mm Hg)}$; $\mathrm{PVO}_2 = \text{uncorrected mixed venous oxygen tension (mm Hg)}$; 0.003 = solubility coefficient of oxygen at 37°C.

All data are presented as mean $\pm$ SD. Analysis of variance was used to compare the mean values at the different perfusion flows.

Regression analysis was conducted between the different perfusion flows and $\mathrm{PVO}_2$, $\mathrm{SVo}_2$, and $\mathrm{VO}_2$ values in both the $\alpha$-stat and pH-stat groups. Also, the $\mathrm{SVo}_2$ value was correlated with the corresponding $\mathrm{PVO}_2$ value to construct an oxyhemoglobin dissociation curve. As the oxyhemoglobin dissociation curve is sigmoid, correlation of $\mathrm{PVO}_2$ and $\mathrm{SVo}_2$ was conducted by correlating log $\mathrm{PVO}_2$ with the probit of $\mathrm{SVo}_2$. The log-probit transformation straightens the sigmoid curve (15) and facilitates the determination of P50 values. The $t$-test of significance was used to compare the slopes ($b$) and intercepts ($a$) of regression lines. Significant results were identified when the $F$ ratio deviated significantly from 1, the null hypothesis of no difference. $P < 0.05$ was considered significant.
Table 1. Mean Temperature-Corrected and Uncorrected pHa and Paco₂ at the Different Perfusion Flows in the α-Stat Group and the pH-Stat Group

<table>
<thead>
<tr>
<th>Flow index (L·min⁻¹·m⁻²)</th>
<th>Paco₂ (mm Hg)</th>
<th>pHa</th>
<th>Paco₂</th>
<th>pHa</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Uncorrected</td>
<td>Corrected</td>
<td>Uncorrected</td>
<td>Corrected</td>
</tr>
<tr>
<td>2.4</td>
<td>37.2 ± 4.6</td>
<td>24.6 ± 3.5</td>
<td>7.42 ± 0.05</td>
<td>7.55 ± 0.06</td>
</tr>
<tr>
<td>1.8</td>
<td>33.8 ± 3.6</td>
<td>22.4 ± 3.7</td>
<td>7.45 ± 0.05</td>
<td>7.58 ± 0.06</td>
</tr>
<tr>
<td>1.2</td>
<td>32.9 ± 3.3</td>
<td>21.9 ± 3.0</td>
<td>7.47 ± 0.04</td>
<td>7.59 ± 0.06</td>
</tr>
</tbody>
</table>

Decrementing of the perfusion flow index from 2.4 to 1.8 and 1.2 L·min⁻¹·m⁻² did not result in a significant change of Paco₂ and pHa in both the α-stat and pH-stat groups (P < 0.05).

Results

In the α-stat groups, the mean value of the temperature-uncorrected pHa was 7.42 ± 0.05 and of the temperature-uncorrected Paco₂ 37.2 ± 4.6 mm Hg. In the pH-stat group, the corrected pHa was 7.40 ± 0.03 and the corrected Paco₂ was 36.5 ± 2.9 mm Hg. In both groups, decreasing the perfusion flow from 2.4 to 1.8 and 1.2 L·min⁻¹·m⁻² was not followed by any significant change in pHa or Paco₂ (Table 1).

In all patients, decreasing the perfusion flow was followed by a significant decrease of SVO₂ (Figure 1) and PVO₂ (Figure 2). The SVO₂ and PVO₂ changes were not significantly different whether α-stat or pH-stat strategy was used.

Correlation and regression of the probit of SVO₂ on the log of the corresponding PVO₂ did not significantly differ in the α-stat group from the pH-stat group (Figure 3). Estimation of the P50 from the regression lines showed a P50 of 11.9 mm Hg in the α-stat group, and a P50 of 12.1 mm Hg in the pH-stat group.

The VO₂ value in both the α-stat and pH-stat groups was not significantly different when a perfusion flow of 2.4 L·min⁻¹·m⁻² was used and did not
show any significant change when the flow was decreased to 1.8 and 1.2 L-min⁻¹-m⁻² (Figure 4).

The data from which the whole-body oxygen consumption was calculated are shown in Table 2.

Discussion

The acid-base management during hypothermic CPB has been controversial (1-3). Two approaches have been advocated. The α-stat strategy aims to maintain the temperature-uncorrected pHₐ near 7.4 and the uncorrected Paco₂ near 40 mm Hg. The second strategy is the pH-stat, which maintains the temperature-corrected pHₐ and Paco₂ near these levels (5). In our first group of patients, the mean temperature-uncorrected pHₐ was 7.42 ± 0.05 and the mean uncorrected Paco₂ was 37.2 ± 4.6 mm Hg, which match the α-stat strategy. In the second group, the mean temperature-corrected pHₐ was 7.40 ± 0.03 and the mean corrected Paco₂ was 36.5 ± 2.9 mm Hg, which match the pH-stat strategy. Changing the perfusion flow in both groups while keeping the oxygen flow constant does not result in any significant change of pHₐ or Paco₂, suggesting that perfusion flow is not the predominant factor determining Paco₂ during CPB.

In both the α-stat and the pH-stat groups, the perfusion flow during CPB is altered sequentially to construct an oxyhemoglobin dissociation curve by correlating the subsequent changes of SvO₂ with the corresponding PvO₂ values. In both groups, decreasing the perfusion flow from 2.4 to 1.8 and 1.2 L-min⁻¹-m⁻² is followed by a significant decrease of 50ₚ and PvO₂, denoting increased hemoglobin desaturation when the perfusion flow is decreased (9). The SvO₂ and PvO₂ values at the different perfusion flows are not significantly different whether pH-stat or α-stat strategy is used. Also, correlation and regression of SvO₂ values achieved at the different perfusion flows with the corresponding PvO₂ values overlaps in the two groups, and shows a P50 of 11.9 mm Hg in the α-stat group and a P50 of 12.1 mm Hg in the pH-stat group (not significantly different). These values are significantly lower than the standard normothermic P50 value of 27 mm Hg, confirming the leftward shift of the oxyhemoglobin dissociation curve by hypothermia (4). However, the similar P50 value in both the α-stat and pH-stat groups is unexpected in view of the known effect of pH and Paco₂ on the oxyhemoglobin dissociation.
Table 2. Data From Which the Whole-Body Oxygen Consumption Was Calculated at the Different Perfusion Flows in Both the $\alpha$-Stat and pH-Stat Groups

<table>
<thead>
<tr>
<th>Flow (L·min$^{-1}$·m$^{-2}$)</th>
<th>$P_{\text{VO}_{2}}$</th>
<th>$S_{\text{VO}_{2}}$</th>
<th>$P_{\text{O}_{2}}$</th>
<th>$S_{\text{O}_{2}}$</th>
<th>Hct</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\alpha$-Stat</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.4</td>
<td>85.0 ± 32.3</td>
<td>91.2 ± 3.7</td>
<td>474.4 ± 121.3</td>
<td>99.87 ± 0.09</td>
<td>23.9 ± 3.5</td>
</tr>
<tr>
<td>1.8</td>
<td>62.5 ± 13.1</td>
<td>86.2 ± 4.6</td>
<td>524.3 ± 133.6</td>
<td>99.39 ± 1.58</td>
<td>23.9 ± 3.5</td>
</tr>
<tr>
<td>1.2</td>
<td>44.9 ± 6.5</td>
<td>73.8 ± 5.8</td>
<td>450.5 ± 106.2</td>
<td>99.88 ± 0.04</td>
<td>23.9 ± 3.5</td>
</tr>
<tr>
<td>$P = 0.0007$</td>
<td>$P &lt; 0.00001$</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>pH-Stat</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.4</td>
<td>98.1 ± 32.4</td>
<td>94.1 ± 3.0</td>
<td>486.9 ± 89.3</td>
<td>99.87 ± 0.06</td>
<td>24.1 ± 2.9</td>
</tr>
<tr>
<td>1.8</td>
<td>69.8 ± 21.6</td>
<td>88.0 ± 5.5</td>
<td>520.9 ± 86.2</td>
<td>99.89 ± 0.03</td>
<td>24.1 ± 2.9</td>
</tr>
<tr>
<td>1.2</td>
<td>65.7 ± 17.5</td>
<td>79.0 ± 7.3</td>
<td>548.7 ± 81.3</td>
<td>99.9 ± 0.00</td>
<td>24.1 ± 2.9</td>
</tr>
<tr>
<td>$P = 0.0129$</td>
<td>$P &lt; 0.00001$</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td></td>
</tr>
</tbody>
</table>

$P_{\text{VO}_{2}}$, temperature-uncorrected venous oxygen tension; $S_{\text{VO}_{2}}$, mixed venous oxyhemoglobin saturation; $P_{\text{O}_{2}}$, temperature-uncorrected arterial oxygen tension; $S_{\text{O}_{2}}$, arterial oxyhemoglobin saturation; Hct, hematocrit percentage.

The $P_{\text{O}_{2}}$ and $S_{\text{O}_{2}}$ values did not significantly change (NS) with changing perfusion flow, whereas $P_{\text{VO}_{2}}$ and $S_{\text{VO}_{2}}$ decreased significantly with decreasing flow ($P < 0.05$).

If blood is cooled in a sealed environment (16), the oxyhemoglobin dissociation curve is shifted to the left secondary to lowering of temperature by about 5.7% per °C, while the increase in affinity of hemoglobin for oxygen owing to the rise in pH is only 1.7% per °C. It is possible that during hypothermia, the effect of cooling on the oxyhemoglobin dissociation overshadows the effect of pH and $P_{\text{CO}_{2}}$ within the range difference between the pH-stat and the $\alpha$-stat groups. Also, Bickler (17) recently found in lizards that the intracellular pH of brain stayed constant over an 18–35°C temperature range (i.e., pH-stat), whereas other tissue compartments including blood conformed to the $\alpha$-stat model. These data point out that intracellular acid-base regulation can be independent of blood regulation and does not always follow $\alpha$-stat (1). This may apply to the intracellular pH of red blood corpuscles and may minimize the effect of pH-stat versus $\alpha$-stat on oxyhemoglobin dissociation during hypothermia.

Despite the leftward shift of the oxyhemoglobin dissociation curve by hypothermia, the whole-body oxygen consumption does not significantly change when the perfusion flow is decreased as low as 1.2 L·min$^{-1}$·m$^{-2}$, whether pH-stat or $\alpha$-stat strategy is used. This may be attributed to the decrease of whole-body oxygen consumption during hypothermia by about 50% for every 10°C decrease in body temperature (18,19). Also, the degree of leftward shift of the oxyhemoglobin dissociation curve by hypothermia is about 7.4% per °C, which is approximately equal to the decrease of $P_{\text{O}_{2}}$ secondary to its increased oxygen solubility (20). The increased solubility of oxygen in plasma by cooling is associated with a concomitant increased affinity of hemoglobin and tissues for oxygen to the same degree, and hence the oxygen diffusion gradient and oxygen delivery may not be impaired (17).

During normothermia, oxygen consumption at stable conditions is equal to oxygen demand. When the oxygen supply (product of cardiac output and arterial oxygen content) decreases to below a critical value, oxygen extraction becomes less efficient, so that the oxygen consumption starts to decrease and becomes supply-dependent (21). The critical level of oxygen supply during normothermia is about 8–10 mL·kg$^{-1}$·min$^{-1}$ (22). This may not apply to hypothermia. In our patients during hemodilutional hypothermic CPB, the oxygen consumption is not decreased despite decreasing the perfusion flow to 1.2 L·min$^{-1}$·m$^{-2}$. The oxygen supply under these conditions is approximately 2–3 mL·kg$^{-1}$·min$^{-1}$. Thus, hypothermia does not impair oxygen delivery whether $\alpha$-stat or pH-stat is used and may even increase the safety margin and decrease the critical oxygen supply necessary to maintain the required oxygen demand.

In conclusion, oxyhemoglobin dissociation and whole-body oxygen consumption are not significantly different between the $\alpha$-stat and the pH-stat groups during hypothermic CPB. In both groups, the dissociation curve is shifted to the left, but the $\dot{V}_{\text{O}_{2}}$ does not significantly change despite decreasing the perfusion flow to as low as 1.2 L·min$^{-1}$·m$^{-2}$. The results suggest that oxygen delivery is not impaired during moderate hypothermic CPB whether pH-stat or $\alpha$-stat strategy is used.

References

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