Jugular Venous Oxygenation During Hypothermic Cardiopulmonary Bypass in Patients at Risk for Abnormal Cerebral Autoregulation: Influence of $\alpha$-Stat Versus pH-Stat Blood Gas Management

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In a prospective, randomized study of cardiac surgical patients at risk for impaired cerebral blood flow autoregulation, we compared $\alpha$-stat and pH-stat blood gas management. The 40 patients enrolled had age $>70$ yr, diabetes, prior stroke, or uncontrolled hypertension. During hypothermia and early rewarming, jugular oxygen tensions were significantly lower in $\alpha$-stat patients ($n=12$) than pH-stat patients ($n=19$; $P<0.05$). During rewarming, jugular venous desaturation (i.e., $S_{jvO_2}<50\%$) occurred in 6 of 12 $\alpha$-stat patients, but no pH-stat patients ($P=0.0006$). Patients at risk for poor cerebral autoregulation have higher oxygen tensions and saturations if pH-stat blood gas management is used during cardiopulmonary bypass.


In patients undergoing coronary artery bypass grafting with cardiopulmonary bypass (CPB), jugular bulb (JB) venous oxygen saturation ($S_{jvO_2}$) typically decreases during rewarming.¹⁻⁶ It has been reported that patients who experience JB desaturation (i.e., $S_{jvO_2}<50\%$) during rewarming have an increased risk of postoperative cognitive deficits.²⁻⁵ Studies in both laboratory animals⁷ and patients¹ have revealed that JB desaturation occurs during rapid rewarming because of an increase in cerebral metabolic rate that is temporarily unmatched by an increase in cerebral blood flow (CBF). Patients in whom desaturation develops may have limited cerebral autoregulatory reserve.²⁻⁴,⁸ Data suggest that patients older than 70 yr and those with diabetes, prior stroke, or abnormalities seen on preoperative brain imaging have lower $S_{jvO_2}$ than patients without these risk factors.⁵,⁸⁻¹⁰ Notably, in most reported series, $\alpha$-stat blood gas management was used.¹⁻¹⁰

While collecting pilot data for our previous study of JB temperature gradients,¹¹ we noticed that JB desaturation did not occur in any patient during CPB with pH-stat blood gas management. Previously, Hanel et al.³ studied 20 low-risk patients managed with the $\alpha$-stat technique and found that desaturation commonly occurred during rewarming with “normocapnia” but was prevented by mild hypercapnia. Because patients with impaired cerebral autoregulation are most likely to develop desaturation, we compared the pH-stat and $\alpha$-stat techniques in such patients. We hypothesized that pH-stat management, which results in a higher partial pressure of arterial carbon dioxide during CPB than does $\alpha$-stat management, would prevent JB desaturation.

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METHODS

After IRB approval and written informed consent were obtained, 40 coronary artery bypass grafting patients with age >70, diabetes, prior stroke, or poorly controlled hypertension (defined as preoperative systolic blood pressure >160 mm Hg despite preoperative use of oral antihypertensive drugs) were assigned to α-stat or pH-stat blood gas management by computer-generated random allocation. Perfusionists and study personnel were blinded to whether blood gases were temperature-corrected (pH-stat) or uncorrected (α-stat).

After anesthetic induction, a 5F thermistor catheter (7.5-cm catheter, model #132PS; Edwards Lifesciences, Irvine, CA) was inserted retrograde into the right internal jugular vein until resistance was encountered, then retracted until blood could be aspirated. No special methods (e.g., fluoroscopy) were used to ensure exact catheter placement. Blood samples were obtained before CPB (during incision and cannulation), every 3 min during CPB, and after CPB (during decannulation and closure) to measure temperature-corrected JB venous (PjvO₂) and arterial (PaO₂ and Paco₂) blood gases (Nova Stat Profile Ultra™; Nova Biomedical, Waltham, MA), according to the temperature measured in the nasopharynx. The degree of induced hypothermia during CPB was selected by each surgeon (range, 28–32°C). Patients were rewarmed to a target nasopharyngeal temperature of 37°C before the end of CPB, but the temperature of the CBP perfusate never exceeded 38°C. PjvO₂ was measured with a co-oximeter (AVOX 4000™; Diametrics Medical, St. Paul, MN).

Blood gases were managed by adjusting the total gas inflow rate to the oxygenator (i.e., the “sweep speed”) using two ventilating gases, O₂ and air. No extraneous O₂ was added. Because perfusionists were not informed about whether the measured blood gas results were temperature-corrected or temperature-uncorrected, one investigator (LRH) checked arterial blood gases at the time of data entry to verify that the perfusionist had successfully adhered to the a priori criteria for α-stat or pH-stat management throughout the study period. These criteria stipulated a temperature-uncorrected Paco₂ of 33–47 mm Hg for the α-stat technique and a temperature-corrected Paco₂ of 33–47 mm Hg for the pH-stat technique. Patients with >1 value outside this range (4 α-stat and 3 pH-stat patients) were excluded. Additionally, one α-stat and one pH-stat patient were excluded because of missing arterial data. Of the remaining 31 patients, 12 were assigned to the α-stat group and 19 to the pH-stat group.

Patients were observed for any overt neurologic abnormalities, transient or persistent, until hospital discharge. Research nurses blinded to group assignment interviewed patients at least once during postoperative hospitalization and retrieved medical records after discharge, including progress notes, consultations, and neurologic studies.

Statistical analysis was performed with SPSS software. Differences between pH-stat and α-stat group measurements were analyzed with t-tests, and adjustments were made with the false discovery rate. For each patient, the lowest SjvO₂ value was categorized as above or below 50%, and the lowest temperature-corrected PjvO₂ was categorized as above or below 30 mm Hg. These categorical variables were assessed with χ² tests.

RESULTS

Neither demographic nor perioperative factors differed between groups (Table 1). Mean temperature-corrected PjvO₂ and mean SjvO₂ were significantly lower in the α-stat group throughout hypothermia and the first minute of rewarming (P < 0.05; Figs. 1 and 2) (Table 2). In α-stat patients, 9 of 12 had at least one temperature-corrected PjvO₂ <30 mm Hg, compared to 3 of 19 pH-stat patients (P = 0.001). The pH-stat group had higher SjvO₂ than the α-stat group during hypothermia (88.5 ± 5.1% vs 75.2 ± 7.3%, P < 0.0001) and during rewarming (76.6 ± 10.3% vs 67.7 ± 14.6%; P < 0.0001). During rewarming, JB desaturation (i.e., SjvO₂ <50%) occurred in 6 of 12 α-stat patients, including 5 diabetic patients, but no pH-stat patients (P = 0.0006).

Late-onset stroke, confirmed by brain imaging, developed in one pH-stat patient on postoperative day 3. Encephalopathy with electroencephalographic abnormalities developed in one α-stat patient. Confusion developed in three pH-stat patients and one α-stat patient.

DISCUSSION

This was the first study of patients at high risk for impaired cerebral autoregulation undergoing CPB with α-stat versus pH-stat blood gas management. Those undergoing α-stat management had temperature-corrected PjvO₂ <30 mm Hg and JB desaturation (SjvO₂ <50%) significantly more often than patients with pH-stat management.

The main difference between these techniques is that pH-stat management produces higher Paco₂ values and, presumably, increased CBF. Thus, pH-stat management may result in more homogenous brain cooling and, consequently, greater reduction of oxygen consumption and better cerebral tissue oxygenation. However, CBF is dependent upon arterial blood pressure during pH-stat management. It has been suggested that partial loss of cerebral autoregulation with pH-stat management may result in a cerebral “steal” phenomenon in patients with cerebrovascular disease and that increased CBF during CPB may result in an increased embolic load, thus potentially increasing the risk of cerebral injury.
Traditional thinking holds that α-stat management better preserves cerebral flow-metabolism coupling and autoregulation of the cerebral vasculature and that, during hypothermia, decreased cerebral metabolic demand and unchanged CBF cause SjvO₂ to increase, indicating “luxury perfusion.” However, higher SjvO₂ at colder temperatures may instead reflect an increased affinity of hemoglobin for oxygen, impairing oxygen transfer to brain tissue, so that less oxygen is consumed than is needed. In fact, a high SjvO₂ during hypothermia may falsely indicate good cerebral oxygenation when, in reality, neuronal hypoxia may be developing.

Therefore, because interpreting SjvO₂ during hypothermia is difficult, we also measured temperature-corrected PjvO₂. Although desaturation never occurred during hypothermia, temperature-corrected PjvO₂ < 30 mm Hg occurred frequently in α-stat patients. Notably, however, both SjvO₂ and PjvO₂ are global, rather than regional, measures of cerebral oxygenation.

Table 1. Patient Demographics, Preoperative Risk Factors, and Perioperative Factors

<table>
<thead>
<tr>
<th>Blood gas management</th>
<th>α-stat (n = 12)</th>
<th>pH-stat (n = 19)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic data</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Mean age (yr)</td>
<td>63 ± 13</td>
<td>69 ± 9</td>
<td>0.19</td>
</tr>
<tr>
<td>Mean weight (kg)</td>
<td>81 ± 15</td>
<td>89 ± 20</td>
<td>0.25</td>
</tr>
<tr>
<td>Mean height (cm)</td>
<td>173 ± 10</td>
<td>173 ± 9</td>
<td>0.85</td>
</tr>
<tr>
<td>Gender (n [%] male)</td>
<td>9 [75%]</td>
<td>14 [74%]</td>
<td>0.80</td>
</tr>
<tr>
<td>Preoperative risk factors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes (n [%])</td>
<td>7 [58%]</td>
<td>12 [63%]</td>
<td>0.79</td>
</tr>
<tr>
<td>Age &gt;70 yr (n [%])</td>
<td>4 [33%]</td>
<td>8 [42%]</td>
<td>0.63</td>
</tr>
<tr>
<td>Prior stroke (n [%])</td>
<td>3 [25%]</td>
<td>2 [16%]</td>
<td>0.53</td>
</tr>
<tr>
<td>Hypertension (n [%])</td>
<td>9 [75%]</td>
<td>15 [79%]</td>
<td>0.80</td>
</tr>
<tr>
<td>Distribution of preoperative risk factors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with only 1 risk factor (n [%])</td>
<td>3 [25%]</td>
<td>4 [21%]</td>
<td>0.70*</td>
</tr>
<tr>
<td>Patients with 2 risk factors (n [%])</td>
<td>8 [67%]</td>
<td>12 [63%]</td>
<td>0.63</td>
</tr>
<tr>
<td>Patients with 3 risk factors (n [%])</td>
<td>0 [0%]</td>
<td>2 [11%]</td>
<td>0.53</td>
</tr>
<tr>
<td>Patients with 4 risk factors (n [%])</td>
<td>1 [8%]</td>
<td>1 [5%]</td>
<td>0.53</td>
</tr>
<tr>
<td>Perioperative measurements</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypothermic temperature during stable hypothermia (°C)</td>
<td>29.4 ± 1.1</td>
<td>29.7 ± 0.7</td>
<td>0.46</td>
</tr>
<tr>
<td>Hemoglobin level during stable hypothermia (g/dL)</td>
<td>7.0 ± 1.4</td>
<td>6.6 ± 0.8</td>
<td>0.24</td>
</tr>
<tr>
<td>Hemoglobin level during rewarming (g/dL)</td>
<td>7.7 ± 1.2</td>
<td>7.2 ± 0.8</td>
<td>0.10</td>
</tr>
<tr>
<td>Arterial blood pressure during stable hypothermia (mm Hg)</td>
<td>53.5 ± 18.4</td>
<td>52.5 ± 11.1</td>
<td>0.85</td>
</tr>
<tr>
<td>Arterial blood pressure during rewarming (mm Hg)</td>
<td>58.0 ± 15.4</td>
<td>61.3 ± 15.0</td>
<td>0.48</td>
</tr>
<tr>
<td>Pump flow during stable hypothermia (mL·kg⁻¹·min⁻¹)</td>
<td>52.0 ± 3.7</td>
<td>54.1 ± 5.7</td>
<td>0.25</td>
</tr>
<tr>
<td>Pump flow during rewarming (mL·kg⁻¹·min⁻¹)</td>
<td>50.6 ± 2.6</td>
<td>53.2 ± 5.9</td>
<td>0.12</td>
</tr>
<tr>
<td>Duration of cross-clamping (min)</td>
<td>37.1 ± 13.0</td>
<td>34.4 ± 13.8</td>
<td>0.66</td>
</tr>
<tr>
<td>Duration of cardiopulmonary bypass (min)</td>
<td>68.0 ± 21.3</td>
<td>71.4 ± 23.4</td>
<td>0.68</td>
</tr>
</tbody>
</table>

Data are reported as means ± SD unless otherwise indicated.

* Single P value for the 2 × 4 subtable.

Figure 1. Temperature-corrected measurements of O₂ tension for jugular bulb venous blood (PjvO₂) in the α-stat group and the pH-stat group are depicted at 3-min intervals during the periods of cooling and stable hypothermia, followed by the rewarming and post-CPB periods. *Indicates P < 0.05. CPB = cardiopulmonary bypass.
pressure, and hemoglobin) during CPB, and imprecise measures of neurologic and cognitive outcomes. Also, the JB catheter position was not confirmed (so that samples could have been contaminated with extracranial blood), and no other measures of cerebral oxygenation were used.

Despite these limitations, it seems that patients at high risk for poor cerebral autoregulation have higher oxygen tensions and saturations during CPB if pH-stat blood gas management is used instead of α-stat management.

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