A Method for the Control of Severe Alterations in Acid-Base Equilibrium

By DOUGLAS MOORE, M.B., and WILLIAM F. BERNHARD, M.D.

COMPLETE operative repair of complex congenital cardiac anomalies frequently requires extended periods of extracorporeal circulation. If, during the prolonged perfusion period, tissue oxygenation becomes inadequate, a progressive metabolic acidosis develops with reductions in arterial pH and plasma bicarbonate. In the majority of such instances, the maximal alterations in acid-base equilibrium occur in the terminal phase of bypass and, therefore, cardiac resuscitation must be accomplished in the presence of a low pH and a depleted intrinsic buffering capacity. Under these conditions, the restoration of an effective cardiac output and ultimate patient survival depend upon prompt and adequate correction of the acidotic state.

Previous clinical experience indicates that an organic hydrogen-ion acceptor, 2-amino-2-hydroxymethyl-1,3-propanediol (tris buffer), is the most effective buffering agent now available.1-3 It is capable of modifying both intracellular and extracellular pH, and is not dependent for effect upon the presence of a normal alveolar exchange. The present investigation involves the use of this agent in: (1) selected patients undergoing prolonged periods of perfusion to permit open repair of a variety of intracardiac defects; (2) the treatment of two patients who developed acute respiratory acidosis in the immediate postperfusion period; and (3) cardiac resuscitation in a patient who experienced a prolonged period of cardiac arrest during an extracardiac operative procedure.

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Material and Methods

Twenty-seven of the 30 patients included in this investigation were selected because it appeared that repair of the existing intracardiac abnormalities would require an extended period of infusion. In each operation (performed under hypothermic cardioplegia), blood samples were obtained from the pump-oxygenator priming blood before and after the addition of tris buffer (400 mg./500 ml. blood). The prime used in each case consisted of heparinized blood collected 24 hours preoperatively and stored at 4°C until used.

In all patients, arterial specimens were obtained: (1) before commencement of bypass; (2) approximately 20 minutes prior to the termination of perfusion; (3) at the conclusion of bypass and at intervals of one, three, and six hours postoperatively (specimens 4, 5, 6).

Blood samples were drawn anaerobically into heparinized, oiled syringes and the following determinations performed: arterial pH, plasma CO₂ content, CO₂ combining power, and plasma lactate. In addition, the partial pressure of carbon dioxide (expressed in mm. Hg) was calculated at 37°C by means of the Henderson-Hasselbalch equation (pK₁ = 6.10). At reduced body temperatures, pCO₂ was computed from the Severinghaus-Stuffle nomogram using values for pK₁ of 6.10 to 6.30.

Twenty-seven cases were divided into two groups for evaluation. Sixteen patients (group I) received tris buffer in the pump-priming blood prior to initiation of bypass, to counteract the low pH of this 24-hour-old perfusate. Although the mean duration of perfusion here was 94 minutes (range, 75 to 166 minutes), none of the patients in this group developed a significant degree of acidosis during perfusion or in the immediate postoperative period.

Group II was comprised of 11 patients who, despite addition of buffer to the pump-priming blood, developed an acute metabolic acidosis during longer periods of perfusion (mean duration, 120 minutes). All cases were treated by the administration of additional tris buffer, 150 mg./Kg. body weight (via the receiving reservoir of the oxygenator), approximately 20 minutes prior to termination of extracorporeal circulation.

Two patients who developed severe respiratory acidosis in the immediate postperfusion period were also included in the study. In each case,
Table 1
Mean Data Obtained from a Study of 200 Pints of Twenty-four-Hour-Old Heparinized Donor Blood Before and After Addition of Tris Buffer (400 mg./500 ml. Blood)

<table>
<thead>
<tr>
<th></th>
<th>Prebuffer</th>
<th>Postbuffer</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH units</td>
<td>7.22</td>
<td>7.42</td>
</tr>
<tr>
<td>Plasma lactate, mM/L.</td>
<td>4.5</td>
<td>4.5</td>
</tr>
<tr>
<td>Plasma CO2 content, mM/L.</td>
<td>25</td>
<td>24</td>
</tr>
<tr>
<td>Plasma bicarbonate, mEq./L.</td>
<td>20</td>
<td>21</td>
</tr>
<tr>
<td>pCO2, mm. Hg</td>
<td>68</td>
<td>45</td>
</tr>
<tr>
<td>Serum potassium, mEq./L.</td>
<td>7.3</td>
<td>7.7</td>
</tr>
<tr>
<td>Plasma hemoglobin, mg. per cent</td>
<td>15</td>
<td>18</td>
</tr>
</tbody>
</table>

Treatment with buffer (150 mg./Kg.) was initiated prior to emergency tracheotomy, and resulted in immediate correction of the hypercarbic state.

The final patient developed sudden cardiac arrest during operative division of an aortic-pulmonary fenestra. Resuscitation of this two and a half year old child was finally accomplished after the intracardiac administration of tris buffer.

Results
Biochemical Analysis of Pump-Oxygenator Priming Blood
Mean data derived from investigation of the 24-hour-old heparinized priming blood disclosed a low pH (7.22), an elevated plasma lactate content (4.5 mM/L.), and an increased serum K+ (7.3 mEq./L.) (table 1). The addition of tris buffer (400 mg./500 ml. blood) to this priming volume restored the pH to 7.42, but produced no change in the lactate level.

Group I (Prevention of Metabolic Acidosis)
An evaluation of the 16 patients in this group did not disclose any evidence of acidosis following restoration of the pump-priming blood pH to normal prior to initiation of bypass. The mean arterial pH at the termination of bypass was 7.43 (table 2). One hour postoperatively, the pH fell to 7.30 (coincident with the peak lactate level), but returned to normal at the end of six hours (7.36). The plasma bicarbonate content declined to 15 mM/L. at the end of perfusion, but had increased to 20 mM/L. six hours later.

A progressive rise in plasma lactate concentration occurred throughout the period of bypass, reaching a peak (4.3 mM/L.) at the end of the first postoperative hour. Six hours after operation, the lactate had declined to 2.6 mM/L. The pCO2 dropped slightly during perfusion, and then stabilized in the normal range postoperatively.

Group II (Management of Metabolic Lacticacidosis)
A metabolic acidosis developed during hypothermic perfusion in this group of 11 patients, and was managed by the further administration of tris buffer (150 mg./Kg.) 10 minutes prior to termination of bypass. Immediately prior to treatment, the mean pH in these patients had declined to 7.18, and was accompanied by a sharp increase in plasma lactate content (4.4 mM/L.), a decrease in bicarbonate (14 mEq./L.), and a low pCO2 (table 3).

Following administration of buffer, a prompt rise in pH occurred (7.38), with a corresponding increase in plasma bicarbonate (20 mEq./L.). The maximal lactate concentration was attained one hour postoperatively (6.8 mM/L.) and was accompanied by a temporary fall in pH (7.29). However, by six hours postoperatively, the pH had stabilized at 7.40. Alterations in plasma bicarbonate paralleled the changes in pH, and also returned to the normal range (21 mEq./L.) by the conclusion of the study.

Management of Acute Respiratory Acidosis
Two patients who developed severe respiratory acidosis in the recovery room following open-heart operations were treated with tris buffer administered through an indwelling caval catheter. The pretreatment arterial pH values were 7.13 and 7.20, respectively, and the carbon dioxide tensions were 76 and 68 mm. Hg (table 4). Shortly after the administration of buffer, the pH in both patients increased (7.52 and 7.41) and was complemented by a decline in pCO2 (32 and 44 mm. Hg). There was also an appreciable rise in plasma bicarbonate level, but no change in total CO2 content.

A tracheotomy was subsequently performed in both patients, and the corresponding biochemical data before and after this procedure are included in table 4. The reaccumulated
Table 2

Mean Values for the Sixteen Patients of Group I Who Underwent Cardiopulmonary Bypass for Ninety-four Minutes

<table>
<thead>
<tr>
<th>Sample no.</th>
<th>I Pre-bypass (Control)</th>
<th>II During perfusion (Prebuffer)</th>
<th>III Conclusion of bypass (Postbuffer)</th>
<th>IV Hours postoperatively</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial pH, units</td>
<td>7.38</td>
<td>7.42</td>
<td>7.43</td>
<td>7.30</td>
</tr>
<tr>
<td>Plasma lactate, mM/L.</td>
<td>1.4</td>
<td>3.6</td>
<td>3.9</td>
<td>4.3</td>
</tr>
<tr>
<td>Plasma bicarbonate, mEq./L.</td>
<td>18</td>
<td>16</td>
<td>15</td>
<td>17</td>
</tr>
<tr>
<td>pCO₂, mm. Hg</td>
<td>48</td>
<td>35</td>
<td>40</td>
<td>45</td>
</tr>
</tbody>
</table>

*There was no evidence of acidosis in this group following the preliminary addition of buffer to the pump-priming blood.

Table 3

Mean Data for the Eleven Patients in Group II Who Developed Metabolic Acidosis During Prolonged Perfusion (Mean, 120 Minutes) Despite Preliminary Buffering of the Pump Prime

<table>
<thead>
<tr>
<th>Sample no.</th>
<th>I Pre-bypass (Control)</th>
<th>II During perfusion (Prebuffer)</th>
<th>III Conclusion of bypass (Postbuffer)</th>
<th>IV Hours postoperatively</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial pH, units</td>
<td>7.54</td>
<td>7.18</td>
<td>7.38</td>
<td>7.29</td>
</tr>
<tr>
<td>Plasma lactate, mM/L.</td>
<td>2.1</td>
<td>4.4</td>
<td>6.1</td>
<td>6.8</td>
</tr>
<tr>
<td>Plasma bicarbonate, mEq./L.</td>
<td>18</td>
<td>29</td>
<td>20</td>
<td>17</td>
</tr>
<tr>
<td>pCO₂, mm. Hg</td>
<td>50</td>
<td>35</td>
<td>37</td>
<td>42</td>
</tr>
</tbody>
</table>

*Prompt restoration of a normal pH and bicarbonate content followed the administration of tris buffer (150 mg./Kg.), despite a further increase in plasma lactate concentration.

Table 4

Effectiveness of Tris Buffer in Treatment of Acute Respiratory Acidosis

<table>
<thead>
<tr>
<th>Arterial pH (units)</th>
<th>Patients 1 and 2 Prebuffer Postbuffer</th>
<th>Patients 1 and 2 Pre-tracheotomy Post-tracheotomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7.13</td>
<td>7.52</td>
</tr>
<tr>
<td>2</td>
<td>7.20</td>
<td>7.41</td>
</tr>
<tr>
<td>Total CO₂ content (mM/L.)</td>
<td>1</td>
<td>22</td>
</tr>
<tr>
<td>Plasma bicarbonate (mEq./L.)</td>
<td>1</td>
<td>14</td>
</tr>
<tr>
<td>pCO₂ (mm. Hg)</td>
<td>1</td>
<td>76</td>
</tr>
<tr>
<td>2</td>
<td>68</td>
<td>44</td>
</tr>
</tbody>
</table>

*Sharp rises in pH and plasma bicarbonate are associated with a decline in pCO₂. Both patients eventually needed tracheotomy (and ventilatory therapy) for persistent respiratory insufficiency.

carbon dioxide was eliminated after the establishment of effective ventilation.

Resuscitation of a Patient After Prolonged Cardiac Arrest

A two and one-half year old (11.0 Kg.) white female child developed refractory ventricular fibrillation during operative closure of a large aortic-pulmonary fenestra performed without pump-oxygenator support. Although some improvement in cardiac tone followed employment of the usual resuscitative measures (transfusion with citrated blood, cardiac massage, and the administration of a variety of stimulating and inotropic drugs),
permanent electrical defibrillation could not be achieved. The effectiveness of cardiac massage during the 90-minute period of arrest was hindered somewhat by the necessity for completing suture lines in the proximal aorta and pulmonary artery.

Cardiac resuscitation was finally accomplished following the intracardiac administration of 2.2 Gm. of tris buffer as a 1.5-M solution. This brought the total amount of buffer used during the period of emergency therapy to 500 mg./Kg. body weight.

No blood specimens were obtained prior to the administration of buffer; however, immediately after resumption of a sinus rhythm, an arterial blood sample revealed a pH of 7.10, a plasma bicarbonate content of 6.0 mM/L., and a plasma lactate of 18.0 mM/L. The addition of a small quantity of sodium bicarbonate (20 mEq.) plus the return of an effective cardiac output raised the arterial pH to 7.35 during the next 30 minutes, and a normal acid-base equilibrium was maintained thereafter.

The patient’s early postoperative course was a stormy one, necessitating tracheotomy, assisted ventilation, and peritoneal dialysis for a period of four days. After this critical phase of convalescence, she steadily improved, and was discharged from the hospital in satisfactory condition three weeks later.

Discussion

Diffuse cellular hypoxia and severe metabolic acidosis may develop during extended periods of cardiopulmonary bypass from the cumulative effect of three factors: (1) the addition of a significant quantity of lactic acid present in the pump-oxygenator priming blood; (2) the development of an oxygen debt in the lean tissue mass which occurs during prolonged hypothermic perfusions; and (3) a reduction in total perfusion flow rate secondary to blood pooling in the splanchnic bed.\(^5\)\(^6\)

Since the rate at which the liver can metabolize excess anaerobic substrates is limited at normal temperature and markedly diminished at temperatures below 30 C., elevated plasma concentrations of a variety of metabolites (predominantly lactate) must be handled by the patient during the terminal stages of bypass and in the immediate postperfusion period.\(^7\) Spontaneous compensation of the lactic acidosis will occur if the cardiac output remains at approximately 2.5 L/min./M.\(^2\). However, if the intracardiac repair is less than adequate, or in the presence of myocardial failure, a diminished cardiac output and further tissue hypoxia will result. Vigorous treatment with an effective buffer must take place at this point if cardiac resuscitation and patient survival are to become a reality.

The development of acute carbon dioxide retention in the immediate postoperative period, secondary to perfusion-induced pulmonary damage, is equally dangerous. Under these circumstances, preliminary treatment of the patient with a buffering agent not dependent upon alveolar gas exchange results in immediate improvement, and permits the performance of tracheotomy under more ideal conditions.

Cumulative clinical experience with tris buffer led us to the development of a two-stage technique for the prevention and treatment of both metabolic and respiratory acidosis. In 16 patients, preliminary neutralization of the increased hydrogen-ion concentration present in the heparinized priming blood sufficed to preserve the patient’s intrinsic buffers for use in compensation of the lactic acidemia noted at the termination of perfusion (group I). In 11 other patients (group II), when the arterial pH and plasma bicarbonate content became markedly reduced prior to the end of bypass, the administration of an additional quantity of buffer to the perfusion system was sufficient to restore acid-base equilibrium.

The final case included in this report illustrates the effectiveness of tris buffer in a very desperate situation. The termination of refractory ventricular fibrillation after a 90-minute period closely followed the intracardiac administration of a large quantity of buffer in concentrated form. Even then, the pH of the arterial blood was only 7.1 units, suggesting
that a considerably lower level was present prior to the administration of buffer. It may be assumed that restoration of cardiac function would not have been possible without the use of buffer in this instance.

Summary

Tris buffer was utilized in the prevention or treatment of profound metabolic acidosis which developed during, and immediately after, extended periods of extracorporeal circulation. In 16 patients (group I), buffer was added to the 24-hour-old heparinized priming blood prior to initiation of bypass, to counteract a low pH and high lactic acid concentration. The success of this therapy was manifested by the stability of all acid-base parameters during and following operation.

In the second group of 11 patients (group II), severe metabolic acidosis developed despite preliminary buffering of the priming blood. Here, the administration of additional buffer successfully restored acid-base equilibrium prior to the termination of perfusion.

The buffer also proved effective in the treatment of two patients who developed severe respiratory acidosis in the immediate postperfusion period, and was instrumental in the resuscitation of a final patient following a prolonged period of cardiac arrest.

It is suggested that tris buffer is a safe, potent agent for use in the prevention and treatment of acidosis from whatever cause.

References


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