Original Article

The Buffering Ability of Commonly Employed Cardiopulmonary Bypass Solutions and Alkalizing Agents

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ABSTRACT

This experiment evaluated the hydrogen ion (H+) buffering capacity (BC) of solutions and alkalizing agents employed during cardiopulmonary bypass (CPB). A solution's BC can be determined when a known quantity of H+ is titrated into the solution and the change (Δ) in pH (log of the hydrogen ion activity ([H+])) is measured (Δ[H+]/mole H+). Eleven solutions were studied: Lactated Ringers (LR), 0.9% NaCl (NS), Plasma-Lyte A™, Hespan™ (6% hetastarch), banked donor blood with citrate phosphate dextrose adenine (CPDA-1), fresh donor blood, THAM™, sodium bicarbonate (NaHCO₃; 1 mEq/ml), high potassium crystalloid cardioplegic solution (HKCCPS), oxygenated crystalloid cardioplegic solution (OCCPS), and adult crystalloid priming solution (AP) per institutional protocol. The solutions were studied at three temperatures: 37°C, 28°C, and 18°C. The null hypothesis stated there was no difference in the BC of the solutions studied. The solutions were first titrated to the same starting pH of 8.0. The solutions were then titrated with a predetermined concentration of hydrochloric acid (HCl) to a pH of 7.0. A higher quantity of H+ added to a solution indicated a greater ability of that solution to buffer H+ within pH limits of 8.0 to 7.0. The data was analyzed with a two way ANOVA and Bonferroni method. A p value <0.05 was considered to be statistically significant. The significant results of our study indicated that THAM™ demonstrated the best BC, followed in decreasing order by NaHCO₃, banked blood, fresh blood, HKCCPS, AP, OCCPS, Plasma-Lyte™, LR, Hespan™, and NS.

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INTRODUCTION

The perfusionist must have an understanding of acid-base chemistry in order to maintain the patient’s normal acid-base status. The occurrence of metabolic acidosis while on cardiopulmonary bypass (CPB) is usually the result of hypoperfusion (1), though it may occur during cooling, rewarming, administration of intravenous solutions, and hypoxia (2-6). Metabolic acidosis is routinely palliated during cardiac surgery by the intravenous administration of sodium bicarbonate (NaHCO₃) (7-9). Various solutions are available to treat an acid-base abnormality. It is the perfusionist’s responsibility to be cognizant of the buffering capacity (BC) of commonly used solutions and alkalizing agents employed during cardiopulmonary bypass (CPB).

One of the major therapeutic characteristics of a solution is its BC (10-14). The BC indicates the solution’s ability to resist a change in pH (15). To quantify a solution’s BC, a known quantity of hydrogen ions (H⁺) can be titrated into the solution and the change (Δ) in pH measured (Δ pH / Δ mmole H⁺) (11,14,16,17) (Figure 1).

A solution’s best BC occurs at its pK. The pK of a solution is the pH at which 50% of the solution (acid or base) is in its protonated form and 50% is in its deprotonated form (i.e. HA⇌ H⁺ + A⁻). Each solution has its own pK, and thus its own unique buffering curve which is graphically represented by plotting percentage dissociation on the Y-axis and pH on the X-axis.

In order for this study to be clinically relevant, we studied solutions over a pH range (7.0 to 8.0) that would encompass normal pH values. In addition, it is understood from basic biochemistry that a change in a solution’s temperature will change the pK of that solution. A change in pK will result in a change in the BC of a solution at the same pH. Perfusionists manage patients on CPB at different temperatures. Therefore, we decided to study the BC of solutions at temperatures used clinically (37, 28, & 18°C).

This study evaluated the H⁺ BC of solutions and alkalizing agents commonly employed during CPB. Knowledge of the BC of these solutions enables the perfusionist to choose a solution which will minimize patient drug administration and work effectively in treating the acid-base disorder, once the cause of the acidosis has been determined (9, 18-20).

The null hypothesis stated there was no difference in the BC of the solutions studied.

METHODS AND MATERIALS

This experiment was designed to determine the BC of eleven solutions at normal physiologic pH and at three temperatures: 37°C, 28°C, and 18°C. The following eleven solutions were studied: lactated Ringers (LR)³; Hespan™ Plasma-Lyte A™; 0.9% NaCl (NS)³; oxygenated crystalloid cardioplegic solution (OCCPS), which consisted of 98.5 ml Ringers, 0.5 meq NaHCO₃, and 1 meq KCl; fresh blood with 3.5 units heparin/ml; banked blood with citrate phosphate dextrose adenine (CPDA-1)³; NaHCO₃; THAM™; high potassium crystalloid cardioplegic solution (HKCCPS), which consisted of 60 meq KCl, 34 ml ACPD³, and 29 ml THAM™ in 500 ml D5W.2NS³; and lastly, adult crystalloid prime (AP) which consisted of 69 ml LR, 28.7 ml Hespan™, and 2.3 meq NaHCO₃.

One hundred ml of each solution was placed in a 200 ml beaker. Each solution was maintained at the desired temperature using an ice bath or a heater/stir plate. Five trials were performed for each solution at each of three temperatures: 37°C, 28°C, and 18°C. The solutions were initially titrated to a pH of 8.0 using a solution of sodium hydroxide (NaOH) or in the case of THAM™, a 12 Normal (N) solution of hydrochloric acid (HCl). The solutions were then titrated with a predetermined concentration of HCl to achieve approximately ten data points between a pH of 8.0 and 7.0. After each addition of HCl the new pH was recorded using a pH meter.

The hydrogen ion activity ([H⁺]ₐ, moles/l) = antilog [-pH] for each solution was plotted against the number of H⁺ (mmole) titrated into the solution ([H⁺]ₐ, moles/l) / mmole H⁺. Five trials, of ten observations each, were used to derive five titration curves. The five titration curves were averaged to obtain one BC curve for each solution at each of the three temperatures. The observed BC were analyzed by two-way ANOVA using statistical software to compare solutions at the three temperatures. A Bonferroni procedure was performed to determine which solutions were different when the ANOVA resulted in the failure to accept the null hypothesis.

RESULTS

Table 1 shows the BC (Δ[H⁺]ₐ, moles/l) / mmole H⁺. The three BC for each solution were then averaged and an overall ranking determined using these averages. The overall ranking was the same as the ranking at 37°C for each solution studied. The seven solutions with the highest BC had the same rank regardless of temperature.
of temperature. There was a difference in the ranking of the last four solutions at 28°C and 18°C. The solutions or alkalizing agents with the highest BC included: THAM™, NaHCO₃, banked blood, fresh blood, HKCCPS, and AP.

The relative overall BC values (Table 2) were obtained by assigning an arbitrary number of 1 to NS. Thus the BC of each solution was compared relative to NS. For example, THAM™ was shown to have \( \times 12,000 \) times the BC of NS.

Blood had the highest BC of the solutions, excluding THAM™ and NaHCO₃. The next three solutions (HKCCPS, AP, and OCCPS) contained THAM™ or NaHCO₃. The alkalizing agent in these three solutions contributed to the BC of each solution was titrated to a lower pH. At a pH of \( \approx 7.0 \), CO₂ began to bubble out of the solution. Therefore, the NaHCO₃ solution was only titrated to a pH of \( \approx 7.2 \).

**DISCUSSION**

Perfusionists are presently using a variety of solutions to prime their cardiopulmonary bypass (CPB) circuits. No one particular solution has been adopted as the "gold standard", or best solution for priming CPB circuits. Failure to adopt a standard priming solution may be due to the number of solutions available; the unique advantages/disadvantages each solution provides, and the lack of scientific information to make an informed decision.

Perfusionists have an obligation to the patient to choose a priming solution with some knowledge of that particular solution's characteristics. Thus, an informed decision can be made regarding the particular advantages/disadvantages a solution affords a patient. Some of the important characteristics are BC, pH, and cost.

### Table 1: Buffering capacity of solutions at all three temperatures.

<table>
<thead>
<tr>
<th>Solution</th>
<th>Overall BC</th>
<th>Avg. BC of all 3 temps</th>
<th>BC at 37°C</th>
<th>Vol. used to titrate to pH=8.0</th>
<th>Hosp. cost of solution (MUSC) ($)</th>
<th>Patient cost of solution (MUSC) ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>THAM™</td>
<td>11,849</td>
<td>8.6</td>
<td>*6.0</td>
<td>0.5</td>
<td>95/500ml</td>
<td>183/500ml</td>
</tr>
<tr>
<td>NaHCO₃</td>
<td>4,743</td>
<td>7.8</td>
<td>0.96</td>
<td>0.1</td>
<td>1.16/500ml</td>
<td>17.00/500ml</td>
</tr>
<tr>
<td>Bk. Blood</td>
<td>536</td>
<td>6.5</td>
<td>0.68</td>
<td>0.07</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Fr. Blood</td>
<td>523</td>
<td>7.4</td>
<td>0.26</td>
<td>0.026</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>HKCCPS</td>
<td>447</td>
<td>7.3</td>
<td>0.27</td>
<td>0.027</td>
<td>115/500ml</td>
<td>258/500ml</td>
</tr>
<tr>
<td>AP</td>
<td>190</td>
<td>7.2</td>
<td>0.23</td>
<td>0.023</td>
<td>29/190ml</td>
<td>41/190ml</td>
</tr>
<tr>
<td>OCCPS</td>
<td>46</td>
<td>7.3</td>
<td>0.03</td>
<td>0.03</td>
<td>2.77/190ml</td>
<td>25.00/190ml</td>
</tr>
<tr>
<td>Plasma-Lyte™</td>
<td>7</td>
<td>7.4</td>
<td>0.004</td>
<td>0.04</td>
<td>2.20/190ml</td>
<td>5.80/190ml</td>
</tr>
<tr>
<td>LR</td>
<td>4.1</td>
<td>6.5</td>
<td>0.005</td>
<td>0.05</td>
<td>1.23/190ml</td>
<td>3.70/190ml</td>
</tr>
<tr>
<td>Hespan™</td>
<td>4</td>
<td>5.5</td>
<td>0.008</td>
<td>0.08</td>
<td>46/500ml</td>
<td>107/500ml</td>
</tr>
<tr>
<td>NS</td>
<td>1</td>
<td>5.0</td>
<td>0.0025</td>
<td>0.025</td>
<td>0.75/190ml</td>
<td>1.95/190ml</td>
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</table>

Overall ranking of the BC of the alkalizing agents and solutions researched from the average of their BC at each of the three temperatures studied (1=highest). The smaller the value \( \Delta [\text{H}^+] \), the greater the BC of that solution. AP=adult prime; BC=buffering capacity; HKCCPS=high potassium crystalloid cardioplegic solution; LR=Lactated Ringers; NS=normal saline; OCCPS=oxygenated crystalloid cardioplegic solution.

### Table 2: Solution characteristics and facts

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<thead>
<tr>
<th>Solution</th>
<th>Relative overall BC</th>
<th>Original pH (pH unit)</th>
<th>NaOH used to titrate to pH=8.0 (mmole)</th>
<th>Vol. used to titrate to pH=8.0 (ml)</th>
<th>Hosp. cost of solution at (MUSC) ($)</th>
<th>Patient cost of solution at (MUSC) ($)</th>
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Data on the 11 solutions studied: Relative BC, starting pH, mmole and ml of NaOH titrated to obtain a starting pH of 8.0, and cost/ml.

*HCl was used to titrate THAM™ to a starting pH of 8.0

1Cost includes: type & screen, x-match, collection, storage, personnel and transfusion.

AP=adult prime; Bk.=banked; BC=buffering capacity, Fr.=fresh, HKCCPS=high potassium crystalloid cardioplegic solution; LR=Lactated Ringers; ml=milliliter; mmole=millimole; MUSC=Medical University of South Carolina; NS=normal saline; OCCPS=oxygenated crystalloid cardioplegic solution; Vol.=volume
Figure 1: Ability of THAM™, NaHCO₃, and fresh blood to buffer H⁺ titrated into solution. There was a significant difference in the BC of each of these solutions \((p<0.05)\).

\[ \text{BC}=\text{buffering capacity, } H^+=\text{hydrogen ion, mmole=millimole} \]

From this study, we found that it would be advantageous to choose a priming solution in regards to its BC.

Our research found that there are significant differences in buffering capacities between all of the solutions we studied except for LR and Hespan™ (Table 1). Also of interest are the differences in starting pH and cost (Table 2). Solutions with a lower starting pH needed the addition of an alkalizing agent to bring the solution to a normal physiological pH. Cost may be a big deterrent, and even the deciding factor, regarding the use of a solution.

The study showed that THAM™ exhibited a BC 2.5 times that of NaHCO₃. Also, unlike NaHCO₃, THAM™ did not decrease significantly in BC as the temperature decreased from 37°C to 18°C. Therefore, THAM™ would be a better alkalizing agent to use in the prime and/or while on CPB to treat an acidotic condition or base deficit. The major disadvantage of THAM™ is its cost and the large volume (500 ml) in which it is sold (Table 2).

This study design provided no respiratory mechanism to blow off the increased production of CO₂ that occurred with the titration of HCl into NaHCO₃. The HCO₃⁻/H₂CO₃ equilibrium equation demonstrates that as additional H⁺ were added, more CO₂ was produced. Thus a point was reached when the solution became saturated with CO₂ resulting in the bubbling of CO₂ out of solution:

\[ \text{H}_2\text{O} + \text{CO}_2 \leftrightarrow \text{H}_2\text{CO}_3 \leftrightarrow \text{H}^+ + \text{HCO}_3^- \]

A pilot study which looked at controlled \((\text{PCO}_2 40 \text{ mmHg})\) versus uncontrolled CO₂ in a solution of NaHCO₃ showed there was no significant difference in the BC when titrated from a pH of 8.0 to 7.2 with HCl.

M.U.S.C. perfusionists presently use LR, Hespan, and NaHCO₃ to prime the CPB circuit. LR and Hespan have a low starting pH, 6.5 and 5.5, respectively. Therefore, the alkalizing agent NaHCO₃ is needed to raise the pH to a normal physiological range. Study results demonstrated that Plasma-Lyte A™ had a better BC and a more physiological pH (7.4) than LR/Hespan™. Plasma-Lyte A™ is also lower in cost than a LR/Hespan™ mixture. Therefore, we recommend the use of Plasma-Lyte A™ instead of LR/Hespan™ because of its pH, lower cost, and greater BC.

Results from this study show that there are significant differences in the BC of solutions commonly employed during CPB. This method of acid titration, at varying temperatures, facilitates the ranking of the BC of solutions and alkalizing agents, including cardioplegic solutions, priming solutions, and blood. The results of this study give the perfusionist the ability to make an informed selection of the optimal solution or alkalizing agent to use while on CPB.

**CONCLUSIONS**

1. THAM™ had the highest BC, followed by NaHCO₃, banked blood, fresh blood, HKCCPS, AP, OCCPS, Plasma-Lyte A™, LR, Hespan™, and NS.
2. As the temperature decreased, the BC of NaHCO₃ decreased.
3. There was no significant difference in the BC of banked blood versus fresh blood, both having the highest BC of all the solutions studied excluding the alkalizing agents, THAM™ and NaHCO₃.

ACKNOWLEDGMENTS

I would like to thank the Extracorporeal Circulation Technology faculty and the Physiology Department faculty at the Medical University of South Carolina for their assistance in the development of the methodology and the data analysis of this study. A special thanks to Dr. Adam Smolka for the use of his lab and to his lab assistant, Peter Zwarych.

REFERENCES