Oxygenation of a Crystalloid Cardioplegic Solution

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Abstract

The purpose of this study is to compare the effectiveness of an alternative method of oxygenating a crystalloid cardioplegic solution to the use of a bubble oxygenator. Five hundred milliliters of 100% oxygen was introduced, using sterile technique, into 100 ml bags of Ringer's solution at varying temperatures (20°, 10°, and 4°C). The contents of the bags were shaken for one minute by hand and then cooled to 4°C or maintained at that temperature using a Shiley CSD 103 Cardioplegia Delivery Set. This method of oxygenation was compared to constant bubbling of 100% oxygen into Ringer's solution in a Shiley S70 bubble oxygenator at 4°C.

Samples of oxygenated solution from the bubble oxygenator were collected over a 60 minute time period. After 30 minutes the values stabilized and the last 12 samples were used as the reference for the bubble oxygenator. Samples of the solutions cooled using the Shiley CSD 103 were taken when the temperature stabilized at 4°C. All 4°C samples were then analyzed for pO2 using an IL 326 blood gas analyzer and the values compared for the various techniques. The results of this study showed the following pO2 values:

<table>
<thead>
<tr>
<th>Method</th>
<th>pO2 (mmHg ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20°C</td>
<td>1183 ± 28</td>
</tr>
<tr>
<td>10°C</td>
<td>795 ± 59</td>
</tr>
<tr>
<td>4°C</td>
<td>983 ± 26</td>
</tr>
<tr>
<td>20°C</td>
<td>1116 ± 18</td>
</tr>
</tbody>
</table>

The conclusion drawn from this study is that the use of Ringer's solution oxygenated and maintained at 4°C is a cost effective alternative to the use of a bubble oxygenator to increase the pO2 in crystalloid cardioplegic solutions.

Introduction

Since 1955, when Melrose, Bentall, and their colleagues introduced the idea of "elective cardiac arrest," cardiothoracic surgeons have been using various cardioplegic solutions for the purpose of inducing cardiac arrest during open heart surgery. Since it was felt that the high potassium cardioplegic solutions did more harm than good to the heart, cardiothoracic surgeons in the United States went for a period of about thirteen years from the early 1960s till 1973 without using cardioplegia during open heart surgery. Cardioplegia use in the United States returned after a study in 1973 by Gay and Ebert on the functional, metabolic, and morphological effects of hyperkalemic crystalloid cardioplegia.

In 1978 Follette and Buckberg suggested the addition of blood to the cardioplegic solution. Theoretically to increase the oxygen carrying capability this blood cardioplegic solution may increase myocardial protection during aortic cross clamping by the release of oxygen carried by the hemoglobin molecules. Another study using blood cardioplegia has suggested any temperature below 20°C actually would reduce the ability of the hemoglobin to release oxygen and therefore the effectiveness of blood cardioplegia. Since 1981, oxygenation of crystalloid solutions has been suggested as an alternative method of providing oxygen to the ischemic myocardium during aortic cross clamping. Three of these studies using blood cardioplegia have suggested any temperature below 20°C would reduce the ability of the hemoglobin to release oxygen and therefore the effectiveness of blood cardioplegia.

By using a bubble oxygenator or a modified cardiomyotomy to oxygenate the crystalloid solution, an additional cost of $100-$300 will be incurred by the patient. In an era of DRGs and a constant attempt to reduce cost, a cost effective method of oxygenating crystalloid cardioplegia would be desirable. The purpose of this study is to develop a comparable method of oxygenating crystalloid cardioplegia and to introduce a cost effective method of oxygenating crystalloid cardioplegia to a known pO2 and oxygen content.

The null hypothesis to be tested is that there is no difference between the pO2 and the oxygen content produced by the methods studied.

Materials and Methods

In this study four methods of preparing oxygenated crystalloid cardioplegia were compared.
Table 1
Uncorrected pO₂ for the Four Methods

<table>
<thead>
<tr>
<th></th>
<th>20°C to 4°C</th>
<th>10°C to 4°C</th>
<th>4°C to 4°C</th>
</tr>
</thead>
<tbody>
<tr>
<td>S70A</td>
<td>12</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>n</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>x mmHg ± SD</td>
<td>1183 ± 28</td>
<td>795 ± 59</td>
<td>983 ± 26</td>
</tr>
</tbody>
</table>

Table 2
Calculated Oxygen Content for the Four Methods

<table>
<thead>
<tr>
<th></th>
<th>20°C to 4°C</th>
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<th>4°C to 4°C</th>
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<td>S70A</td>
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</tr>
<tr>
<td>n</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>x ml/dl ± SD</td>
<td>3.55 ± 0.09</td>
<td>2.38 ± 0.17</td>
<td>2.95 ± 0.07</td>
</tr>
</tbody>
</table>

In the first method 1000ml of Ringer’s Solution (RS) was recirculated and chilled to 5°C at one 1/min through a Shiley S70A bubble oxygenator with an oxygen flow rate of one 1/min. RS was used because it is a balanced electrolyte crystalloid solution typical of those that can be used to make a crystalloid cardioplegic solution. At five minute intervals five samples were drawn and analyzed for pO₂. When there was no measurable change in the pO₂ for three consecutive samples, 12 samples were drawn and recorded.

In the second method four bags of room temperature (20°C) RS were oxygenated in the following manner: Air was removed via a 19ga needle placed into the injection port of the RS bag. Next, using a gas filter, 100% oxygen was bubbled into the bag until the bag became distended (50mmHg). The oxygenated solutions were then shaken by hand for 60 seconds and introduced into a Shiley Cardioplegic Solution Delivery Set CSD-103. The RS was recirculated with the cooling coil submerged in an ice bath till the temperature reached 4°C (a needle probe was inserted into the injection port of the CSD-103 and temperature was monitored by a Tele-thermometer temperature box). Once the desired temperature was reached, three samples from each bag were taken and analyzed for pO₂.

In method three and four, four RS bags were cooled in a refrigerator to 10°C and in ice to 4°C respectively. These bags were then oxygenated and analyzed for pO₂ in the previously described manner.

All samples were analyzed using the IL Micro 13 blood gas analyzer which was calibrated for the higher limit with 95% oxygen and for the lower limit with 20% oxygen to insure accuracy at higher pO₂. All data are reported uncorrected and oxygen contents were calculated from the uncorrected data.

Statistical Analysis
Analysis of variance (p < 0.05) was used to determine statistical significance between the four groups. The Student-t test (p < 0.05) was used to determine statistical significance between methods 2, 3, and 4 and the bubbler method. The IBM Systat® statistical package was used to analyze the data.

Results
The results of this study are summarized in Tables 1 and 2. Note the similarity between the bubbler method and method four.

Analysis of variance indicated there was a statistically significant difference in the methods. The S70A group and the group of 4°C RS maintained at 4°C were significantly different.

Discussion
The advantages of oxygenated crystalloid cardioplegia over nonoxygenated crystalloid cardioplegia have been noted in several studies. Bodenhamer et al observed a significant decrease in the mean postreperfusion adenosine triphosphate (ATP) levels of canine hearts perfused with nonoxygenated crystalloid cardioplegia as compared to the canine hearts perfused with a fully oxygenated solution. Also noted was a significant increase in the myocardial water content in the nonoxygenated group but not in the oxygenated group. Ultrastructural evaluation of these hearts showed severe ischemic damage in the nonoxygenated group as compared to the normal appearance of the oxygenated group.

In 1985 Guyton et al indicated that oxygenation of a crystalloid cardioplegic solution led to an improved recovery of regional function in the left anterior descending and circumflex regions after 15 and 30 minutes of ischemia respectively. This study also noted that the mean 12 hour post operative creatine kinase

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a Travenol Labs, Inc. Deerfield, IL 60015
b Shiley, Inc. Irvine, CA 92714-5751
c Yellow Springs Instrument Co., Inc. Antioch, OH 43710
d Instrumentation Laboratory Inc., Lexington, MA 02173
e Systat, Inc. Evanston, IL 60202
f American Bentley, Irvine, CA 92714
MB level of the nonoxygenated group was more than twice that of the oxygenated group in patients subjected to greater than 28 minutes of aortic cross clamping.\textsuperscript{17}

While comparing an oxygenated crystalloid cardioplegic solution to a blood cardioplegic solution, Heitmiller et al\textsuperscript{19} examined changes in myocardial ATP concentrations and left ventricular function (LVF) during reperfusion. This study concluded that there was no added beneficial effect on LVF by blood cardioplegic solution to a blood cardioplegic solution, Heitmiller et al.\textsuperscript{19} This study concluded that there was no added beneficial effect on LVF by blood cardioplegic solution. 19

In this study RS oxygenated and recirculated through a Shiley S70A bubble oxygenator was compared for pO\textsubscript{2} and oxygen content to 1000 mls of RS which was oxygenated in the prescribed manner. Results of this study indicated that the method of oxygenation in the first method was a comparable method to that used by Bodenhamer et al.\textsuperscript{16} To this method three different treatments of oxygenation using the described technique were compared. Of these three methods the pO\textsubscript{2} and oxygen content of 4°C bags of RS oxygenated and maintained at 4°C were found to be closest to the S70 group. But as previously stated, statistical analysis indicated that there was a statistical difference between these two groups. This was calculated to be a 6% decrease in the pO\textsubscript{2} and the oxygen content of the 4°C maintained group as compared to the S70A group. Since this study did not examine the clinical use of the oxygenated cardioplegia developed by this new technique, the clinical significance was not determined, although we at this institution doubt that any clinical significance exists. Further clinical investigation using this new method of oxygenating crystalloid cardioplegia is warranted.

The cost for a Shiley S70A retails for $280. A new device developed by American Bentley (OxyHi\textsuperscript{TM}) for delivering oxygenated crystalloid cardioplegia retails for $95. The Bentley device claims to deliver an oxygenated crystalloid solution with temperature corrected pO\textsubscript{2}s in the upper 600-smmHg (product information). The cost for the Shiley CSD-103 which was used with the newly developed technique retails for $40.

The conclusion from this study is that the use of RS oxygenated and maintained at 4°C is a cost effective alternative to the use of a bubble oxygenator or other devices to increase the pO\textsubscript{2} and the oxygen content in crystalloid cardioplegic solutions.

![Figure 2: Calculated Oxygen Content of the Four Methods (mean ± SD)](image)

References

Questions from the Audience

**Question**—**Mary Williams**: You said you had so many samples. Where was your sampling site? Was it at the bag or up on the field where the cardioplegia was administered?

**Answer**: In the CSD, Shiley Delivery Set, there is an injection port on top of the bubble trap. That was the site for the injections.

**Question**—**Mary Williams**: Well, after you were administering your cardioplegia, did you ever notice gas coming out of the solution as it travelled up to the patient?

**Answer**: This was not a clinical study. This was all performed in a lab, so there is no patient involvement at all.

**Question**—**Phil Wagoner**: The thought crossed my mind that I would be extremely concerned about cooling my cardioplegia to 4 degrees, and then oxygenating it by any means, and then introducing it to a relatively warmer myocardium, where it would remain in stasis. It seems to me that we'd be in great danger of introducing microair at the microcirculation level, and I think maybe that would be something we'd want to think about before we pursue this in a clinical setting. How many milliliters of oxygen were you able to transfer? Did you do that study by any chance?

**Answer**: No, again, this was done purely in a laboratory. There was no clinical use of this at all.

**Question**—**Sharon Crease**: One of our surgeons had this whim about 1979. We did this procedure for about a year, and at the time, one of our fellows was doing a study. They found absolutely no clinical significance on the patients that had oxygenated crystalloid cardioplegia.

**Response**—**Jim Dearing**: If you were going to deliver crystalloid cardioplegia at 4 degrees, I'd think you would probably, by far, rather have oxygen than air coming out of solution.