An In Vitro Evaluation of a Self-contained Cardioplegia Delivery Device

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ABSTRACT

Focus on improved myocardial protection has prompted the development of delivery systems which can accommodate the demands of increasingly refined cardioprotective strategies. The purpose of this study was to evaluate the Sorin Blood Cardioplegia Console™ (BCC) for accuracy and precision in the delivery of cardioplegia solutions. An in vitro model was designed to evaluate the following performance characteristics of the BCC: delivery volume (blood and crystalloid) at 50, 250, 375, and 500 ml/min flow rates; potassium end-delivery concentration at blood:crystalloid ratios of 4:1, 8:1, and 16:1; intermittent cardioplegia delivery; and heat transfer of the internal heater/cooler.

Differences in blood and cardioplegia volumes between measured and calculated values across all flow rates tested were found to be statistically significant and ranged from 1.4 to 21.5 ml; however, the differences were within the accepted variance of the instrument (±5%). Across all tested ratios, the measured end-potassium concentrations were all within 1 mEq of the expected values, except for the 16:1 ratio at 50 ml/min, which had a 2.52 mEq variance. All significant differences were within the accepted variance of the instrument (±5%). In conclusion, the BCC accurately and delivered cardioplegia volumes and potassium concentrations across all tested conditions with reproducible performance.

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INTRODUCTION

Cardioprotective techniques have undergone an intriguing evolution over the last forty years. Pharmacological cardiac arrest was reported by Melrose et al in 1955 (1), whereby asystole was achieved by delivering a sanguineous potassium citrate solution directly into the coronary circulation. While much has changed in the practice of myocardial management, intraoperative protection has remained paramount for the prevention of irreversible ischemia and reperfusion injury (2). Focus on improved myocardial protection has prompted the development of cardioplegia instrumentation that can accommodate the needs of increasingly sophisticated cardioprotective strategies.

The function of cardioplegia during cardiopulmonary bypass (CPB) is multifactorial, but ultimately it must provide nutrient delivery and produce safe, reversible chemical arrest. A secondary function of cardioplegia delivery is the removal of metabolic intermediates which otherwise could result in the self-pollution of the cellular environment. Pharmacologic arrest reduces metabolic energy requirements, which in the face of inadequate delivery, limits structural derangements to the myocyte (3). The precise delivery of both nutrients and chemicals is crucial to protect the myocardium from ischemic and reperfusion damage (4).

Different cardioplegia additives, methods of delivery, and variations in volume and temperature have all been proposed to improve cardioprotective techniques. Ebert has reported that the choice of cardioplegia solution is less important than the technique of administration and maintenance of hypothermia (5). Controversy exists regarding the optimization of cardioplegia delivery. Various technical comparisons include warm versus cold cardioplegia, antegrade versus retrograde delivery, intermittent versus continuous perfusion, blood versus crystalloid cardioplegia, and hemodilution versus the risk of concentrate overdose (6). Lazar and Roberts have reported that by manipulating the flow, pressure, volume, and distribution of cardioplegia, better intraoperative myocardial protection can be achieved (3). As part of a survey of cardioplegic techniques conducted by Robinson et al in 1992, 936 practicing cardiac surgeons were asked to state important areas of current or future research (7). While the majority responded that they were satisfied with their current method of myocardial protection, 33.9% expressed interest in improving cardioplegia delivery systems.

Most contemporary cardioplegia delivery devices serve a simple three-fold function: mixing blood and crystalloid solutions in fixed ratios, regulating thermal delivery via an integrated heat exchanger, and delivering cardioplegia under pressure to the coronary circulation (8, 9). Although the ultimate reperfusion technique that would optimally protect the myocardium has yet to be established, the need exists for delivery systems that allow for greater flexibility in the administration of cardioplegia (10).

The Blood Cardioplegia Console® (BCC) is a self-contained cardioplegia device that has been developed by Sorin Biomedical®. The purpose of this study was to quantitatively assess the ability of the BCC to accurately and precisely deliver expected volumes and concentrations of cardioplegia solutions over a variety of test conditions.

MATERIALS AND METHODS

DEVICE DESCRIPTION

The BCC a is an integrated cardioplegia delivery system comprised of two 3 in diameter roller pumps, an internal heater/cooler, and monitoring and control systems (11). The console is designed to operate in conjunction with a remote display monitor which consists of a control module and digital display. Standard disposable tubing sets of either 2:1 or 4:1 blood:crystalloid ratios are compatible for use with the BCC. The incorporation of a dual roller pump system into the instrument design facilitates alteration of blood and crystalloid solution ratios, which range from 1:1 through 16:1, or all-blood and all-crystalloid solutions. The BCC can be set to intermittently deliver crystalloid solution during continuous blood delivery.

The BCC is capable of delivering solutions in either a pulsatile or a continuous flow mode. Maximum flow rate for crystalloid solution is 450 ml/min, and for all-blood and all ratios of blood:crystalloid the maximum is 600 ml/min. The minimum flow rate of the BCC is dependent on the tubing set used, with 10 ml/min possible with a 2:1 disposable set, and 20 ml/min delivery when a 4:1 set is used.

The front panel of the BCC contains the major control features of the console. Flow rates, ratios, and volumes of infused blood and crystalloid can be viewed by scrolling through a light-emitting diode menu. Total cardioplegia volume, time intervals, pressures and temperatures are viewed on the remote display monitor. The BCC is equipped with multiple channels for temperature and pressure transducers. Pressure channels are linked to audible and visual alarms, and receive signals from line and delivery points and display them simultaneously. BCC pressure measurement range is from -99 to 500 mmHg (±5 mmHg). Two temperature monitoring channels are available that use commercially available thermometers. The BCC measured temperature range is 0-40°C, ±1°C.

The control panel is hinged to provide access to a self-contained water bath located in the base of the pump. The internal heater/cooler controls the temperature of water delivered to the cardioplegia heat exchanger, allowing adjustments between 0°C and 40°C. The cold water temperature is dependent upon the quantity of ice in the bath.

CIRCUIT PREPARATION

a  Sorin Biomedical, Irvine, CA
b  Stockert Instruments, Munich, Germany
c  Yellow Spring Instruments, Yellow Springs, OH
A model for evaluating mechanical myocardial protection devices has been previously established within our institution (12,13), and was modified for the present study. An extracorporeal circuit was constructed from 1/4 in polyvinylchloride (PVC) tubing (Figure 1). A 20 L plastic container served as a blood reservoir and was connected to a centrifugal pump. Blood from the reservoir was pumped through a stainless steel heat exchanger and then through a 40-micron arterial line filter. A heater-cooler maintained perfusate temperature at 37 ± 1°C. A hemoconcentrator was placed into the arterial filter bypass line with a 1/4 in wye connector and was utilized to adjust the starting hematocrit to 25 ± 2%. Pressure was maintained in the circuit at a constant limit of 100 mmHg with the use of a Hoffman clamp. A 1/4 in wye connector placed distal to the arterial line filter directed the flow to either the reservoir or the blood pump of the BCC.

A 2:1 cardioplegia tubing set was installed on the BCC according to manufacturer’s instructions. The occlusion of the two BCC roller pumps were set at just-occlusive settings at 100% utilizing dual methodology. A 300 mmHg afterload pressure was set by operating each pump against an infinite afterload. Once 300 mmHg was recorded, the occlusion was reduced until pressure began to fall; at that time, the occlusion was adjusted to a just-occluded phase, and the process repeated. The second method involved creating a hydrostatic pressure head of 76 cm H2O between the maximum height of fluid and the reservoir, and measuring the drop in fluid meniscus over one minute. If the fluid level dropped at all, the occlusion was readjusted to a total occlusion set point just above the point where the fluid drop occurred. These occlusion methods were repeated in triplicate for each pump prior to each experiment.

The test circuit was primed with 1700 ml of 0.9% saline solution and thoroughly debubbled. Ten thousand units of heparin were added to the prime. Expired human packed red blood cells, obtained from the University of Nebraska Medical Center blood bank, were washed with physiologic saline solution in an autotransfusion device. Normal saline served as a cardioplegia base solution in the crystalloid pump.

**VOLUMETRIC DETERMINATION**

Volumetric accuracy and precision of the BCC was determined by measuring the volume delivered by the device in timed collections and comparing it to the reported delivery volume from the console. A 1/4 in wye collector placed distal to the outlet line bifurcation directed the flow either to the reservoir or to a graduated cylinder for volume measurement. Volume from the blood and crystalloid pumps was also measured individually by removing the outlet line wye bifurcation on the distal side of the pumps, and connecting a 15 cm length of 1/4 in PVC tubing to the outlet line of each individual pump. The outlets of these added tubing segments were directed into separate graduated cylinders for timed collections. All volumetric determinations were made at 50, 250, 375, and 500 ml/min using a 4:1 blood:crystalloid ratio. Volume samples were taken in quadruplicate and were collected for one minute at each flow rate.

**POTASSIUM CONCENTRATION**

The ability of the BCC to precisely deliver potassium concentration [K+] was evaluated by measuring the delivered concentration and comparing it to an expected concentration of 20 mEq/ml. A real-time gas analyzer was calibrated according to the manufacturer’s specifications, and was used to measure [K+] at the beginning of each set of ratio trials. From this known [K+], a calculated amount of potassium chloride (KCl) was placed into 1 L of 0.9% saline solution to achieve an end-delivery [K+] of 20 mMol. The amount of KCl added to the crystalloid was calculated by solving for the variable in the following formula:

\[
\text{(parts blood)}(\text{[K+] in blood}) + (\text{parts crystalloid})(\text{added mEq of KCl})/\text{total parts} = 20 \text{mMol/L}.
\]

Ratios of 4:1, 8:1, and 16:1 of blood:crystalloid were evaluated at flow rates of 50, 250, 500 ml/min. When a trial was begun at a new flow rate, the circuit was flushed with 250 ml of solution corresponding to the next sample determination. Fluid was collected for 1 min in a graduated cylinder, and samples were taken in quadruplicate at each flow rate.

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d  BP-80, Biocomise 520 D, Biomedicus, Minneapolis, MN
e  Model D1079E, Medtronic Cardiopulmonary Inc., Minneapolis, MN
f  Affinity AT, Acor Cardiovascular, Minneapolis, MN
g  Sorin 3M, Ann Arbor, MI
h  HPH 1000, Minntech Corporation, Minneapolis, MN
i  Vanguard BCD, Sorin Biomedical, Irvine, CA
j  Sorin STAT-P, Sorin Biomedical, Irvine, CA
k  Instrumental Laboratory, Lexington, MA

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INTERMITTENT flow rate. pH measurements from sample volumes collected during a 5 min trial of cardioplegia delivery. Sodium bicarbonate (200 mL) was added to 800 mL of 0.9% saline. During the intermittent crystalloid delivery trials, this bicarbonate solution was used as crystalloid cardioplegia, and a 1 L bag of 0.9% saline was substituted for blood volume. An initial pH measurement of the bicarbonate solution (8.27) and the saline (6.17) were determined using a portable pH meter. To evaluate the intermittent crystalloid delivery function, a 2 1/2 min interval of crystalloid infusion was set over a 5 min period of blood delivery. The blood:crystalloid ratio was set at 4:1, and the cardioplegia flow was 250 mL/min. Samples were collected for 5 sec at 15 sec intervals during a 10 min trial of continuous blood delivery. Each sample was measured for pH, and 3 trials were performed.

**TEMPERATURE**

To assess the accuracy of the BCC in recording blood outlet temperature, temperature readings from a thermistor were compared with BCC temperature recordings. Two calibrated thermisters, one from the BCC and one from a Yellow Springs Instrument (YSI) console, were connected in tandem within 5 cm of another, and were placed 10 cm distal to the outlet of the Blood Cardioplegia Device (BCD). Before the start of each temperature trial, the BCC cooling chamber was filled with ice. Perfusate circulated through the BCD until a starting blood outflow temperature of 37°C ± 1°C was achieved. The BCC console was then set to maximum cool, and temperature readings were recorded from the BCC display and the YSI at 5 sec intervals until 5 consecutive readings of the same temperature were observed from the BCC. At this point, warming was initiated by turning the BCC heater/cooler to 37°C. Temperatures were again recorded at 5 sec intervals until 5 consecutive readings of the same temperature were observed from the BCC. Two trials were performed at flow rates of 50, 250, and 500 mL/min.

**STATISTICS**

All data were recorded in a spreadsheet format on a personal computer and were reported as mean ± standard deviation of the mean. Differences between expected and measured val-

<table>
<thead>
<tr>
<th>Blood Flow Rate (ml/min)</th>
<th>Measured (ml)</th>
<th>Expected (ml)</th>
<th>Difference (ml)</th>
<th>p value</th>
</tr>
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<tbody>
<tr>
<td>50</td>
<td>40.88 ± 0.75</td>
<td>39.75 ± 0.50</td>
<td>1.13 ± 0.48</td>
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<tr>
<td>250</td>
<td>20.25 ± 0.50</td>
<td>19.25 ± 0.50</td>
<td>0.80 ± 0.71</td>
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<tr>
<td>375</td>
<td>32.75 ± 0.63</td>
<td>29.95 ± 1.00</td>
<td>13.25 ± 1.06</td>
<td>0.0001</td>
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<tr>
<td>500</td>
<td>42.00 ± 0.76</td>
<td>40.50 ± 0.58</td>
<td>21.50 ± 5.07</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

<table>
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<tr>
<th>Crystalloid Flow Rate (ml/min)</th>
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<th>Expected (ml)</th>
<th>Difference (ml)</th>
<th>p value</th>
</tr>
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<tr>
<td>50</td>
<td>10.05 ± 0.10</td>
<td>9.75 ± 0.50</td>
<td>0.30 ± 0.48</td>
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</tr>
<tr>
<td>250</td>
<td>49.94 ± 0.13</td>
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<td>375</td>
<td>74.00 ± 0.71</td>
<td>74.75 ± 0.50</td>
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<td>NS</td>
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<tr>
<td>500</td>
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<td>100.00 ± 0.00</td>
<td>-0.05 ± 0.10</td>
<td>NS</td>
</tr>
</tbody>
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Test conditions: 4:1 ratio, pump variance ±5%, p < 0.05

<table>
<thead>
<tr>
<th>Flow Rate (ml/min)</th>
<th>Measured (ml)</th>
<th>Expected (ml)</th>
<th>Difference (ml)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
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<td>250</td>
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<tr>
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<td>0.0001</td>
</tr>
<tr>
<td>500</td>
<td>514.50 ± 1.78</td>
<td>500.50 ± 1.00</td>
<td>14.00 ± 2.48</td>
<td>0.0001</td>
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Test conditions: 4:1 ratio, pump variance ±5%
ues were analyzed with one way analysis of variances using a commercially available statistics program. Statistical significance was accepted at p < 0.05 level.

RESULTS

No differences were observed between expected and measured volumes of crystalloid cardioplegia collected at all flow rates (Table 1). There were statistically significant differences between measured and expected values of blood volumes collected at all measured flows. However, all differences were within the manufacturer's listed variance (±5%) of the roller pump (Table 2). Significant differences between measured and expected [K+] were found at the following ratios and flow rates: 4:1, 500ml/min; 16:1, 50ml/min; and 8:1, 50, 250, and 500ml/min (Figure 2). Again, all significant differences were within the accepted variance of the instrument (±5%).

The function of intermittent cardioplegia delivery was demonstrated by changes in pH samples collected during a 10 min trial of cardioplegia delivery (Figure 3). At the 250 ml/min flow rate, a change in pH was observed approximately 25 sec following the cessation and initiation of the crystalloid pump.

The heat transfer of the BCC internal heater/cooler was also assessed. At a flow of 50 ml/min, the time to cool and rewarmed was 385 sec (Figure 4). As the flow increased to 250 ml/min, the time to cool and rewarmed decreased to approximately 217 sec. As flows increased to 500 ml/min, a 170 sec period to cool and rewarmed was observed.

DISCUSSION

In spite of the technological advances in cardioplegia delivery instrumentation, inadequate myocardial protection is still a primary causative factor of cardiac mechanical failure following cardiac surgery (2). Improved surgical techniques cannot compensate for myocardial damage caused by intraoperative ischemic, hypoxic, or reperfusion injury. Although adequate cardiac preservation is supported by the combined efforts of all individuals on the surgical team, the delivery of cardioplegia is a responsibility ultimately borne by the perfusionist. It is clear that post-cardiotomy myocardial function is critically influenced by a number of factors, including the successful manipulation of cardioplegia delivery.

Although fixed-ratio cardioplegia delivery instrumentation is generally standard within surgical practice, this technology allows little flexibility in changing the ratio of blood:crystalloid components of cardioplegia intraoperatively. Variance in the composition of cardioplegia constituents is achieved by connecting separate bags of base crystalloid solutions that contain specific concentrations of additives. The only change usually possible is the incorporation of higher ratios of blood from the arterial circuit. Increasing the blood:crystalloid ratio will also result in an alteration of end delivery concentration of nutrients, buffers, and ions.

The BCC was designed to facilitate changes in blood:crystalloid ratios during cardioplegia delivery. In order to evaluate the capability of the BCC to accurately deliver set ratios of blood and crystalloid solutions, end-point samples were collected and
analyzed for [K+]. These values were compared to expected values, and statistical differences were demonstrated; however, across all measured ratios, the end [K+] were within 1 mEq of the expected values, except for the 16:1 ratio delivered at 50 ml/min, which had a 2.52 mEq variance.

The capability of the BCC to accurately deliver blood and crystalloid volumes across different flow rates and ratios was also assessed. Despite the presence of statistically significant findings, all measurements were within the tolerance of the instrument. However, our data suggests that the BCC is most accurate at the lower flow rates, since both the blood and the crystalloid volumes demonstrated only minor differences between expected and measured volumes. This is especially important in situations where lower flow rates, such as in pediatric and retrograde administration, are desired. At the flow rates tested, the revolutions per minute (RPM) of the cardioplegia pump were slower than the RPM of the blood pump. Pump rotation at slower rates may allow for more accurate volume delivery.

The BCC function of intermittent crystalloid delivery during continued blood flow was demonstrated through the use of acid-base changes. At a flow rate of 250 ml/min, an observed change in pH occurred approximately 25 sec following the cessation and initiation of the crystalloid pump. This change in pH is a reflection of the washout effect of solution from the circuitry. The pH changes produced were a function of circuit prime volume and flow rate.

In conclusion, our evaluation of the accuracy and precision of the Sorin Blood Cardioplegia Console showed this device to be both precise and accurate in delivering specified volumes and ratios of blood and crystalloid solutions. In addition, the BCC’s mechanical cardioplegia timer and integral heater/cooler proved to be both efficient and reliable.

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REFERENCES