Evaluation of Blood Cardioplegia Administration Systems

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Abstract

Four different blood cardioplegia administration systems (CAS) were evaluated for ease of use, cooling capacity, uniformity of mixing and blood flow capability. The CAS were one single pass (SP) and three recirculating CAS (RC). Each of the RC had a different reservoir; the first a cardiotomy reservoir (CARD), the second a transfer bag, and the third the GISH system.

Each CAS was primed and debubbled with crystalloid. For RC, blood was collected, potassium added, and the solution cooled to 10 °C. With SP, the infusion temperature at the field was measured at different flows and oxygenator temperatures. Hematocrit and potassium were measured at the start and end of cardioplegia administration.

Single pass had the least tubing, lowest priming volume and the simplest design. For RC, 10 °C infusate temperature was obtained fastest with the heat exchanger at the pump outlet and slowest at the reservoir inlet. For SP, the temperature at the field increased as either the oxygenator temperature and/or the cardioplegia flow rate increased. Only RC with CARD produced nonuniform mixing (initial potassium and hematocrit compared to the end of infusion were 16 percent lower and 36 percent higher respectively). At 10 °C infusate temperature, RC allowed higher flow rates than SP. The GISH administration tubing had high resistance (800 mmHg at 500 ml/min).

GISH is flow-limited by resistance and SP by cooling capacity. Clinically, if oxygenator temperature and infusion flows are such that SP can be used it is preferred. Otherwise, RC with low resistance tubing and heat exchanger within the reservoir is optimal.

Introduction

Blood cardioplegia has been shown to be superior to crystalloid in preserving the ischemic myocardium. To administer blood cardioplegia, various techniques have been described ranging from recirculating to single pass circuits. A recirculating system can provide cold blood cardioplegia at any temperature at the point of infusion. However, the adequacy of mixing when the recirculating system uses a cardiotomy reservoir as the blood reservoir has not been demonstrated.

It was the purpose of this work to evaluate the recirculation system made up with a cardiotomy reservoir (RC-CARD) or with a plastic bag reservoir (RC-Bag) and compare them to two commercially available blood cardioplegia systems—the GISH recirculation system (GISH) and the Buckberg-Shiley single pass system (SP). The evaluation consisted of measuring how fast blood cardioplegia is ready for infusion, how cool the solution becomes, how well the blood and cardioplegia additives mix, the perfusion pressure within the delivery set and ease of use.

Material

Recirculation cardioplegia delivery systems that were tested consisted of a reservoir, a pump, a heat exchanger and connecting tubing (Figure 1) in various configurations. Blood was collected in the reservoir, (clamp B, open A), cardioplegia components added, and the mixture recirculated through the heat exchanger, cooled, and returned to the reservoir. To infuse cardioplegia, the patient line was unclamped at C and the recirculation line clamped at D.

For RC-Bag, a 1000 ml plastic bag reservoir (Trans-
The four cardioplegia administration systems were evaluated in vitro for cooling rate, uniformity of mixing, perfusion pressure and ease of use. Heparinized canine blood was used to determine cooling rate and perfusion pressures and heparinized human blood was used to assess uniformity of mixing. The blood was collected from the oxygenator at the end of a clinical (human) or experimental (canine) procedure requiring cardiopulmonary bypass and placed in a 3 liter bag (#2B7127). For RC, the cooling rate was evaluated using 1200 ml of heparinized blood (hematocrit = 15 percent) to prime the circuit and fill the reservoir. The blood was then brought to 37°C, the ice water pump started and the blood pumped at a preselected flow (200 to 670 ml/min). The temperature at the inlet ($T_i$) and outlet ($T_o$) of the heat exchanger were measured with a needle myocardial temperature probe (model #TMPM) connected to a Temperature Monitor. The needle was inserted through the tubing wall and placed in the blood stream. Each probe was calibrated against a mercury thermometer (#T2100-1) that had been checked against a thermometer calibrated by the National Bureau of Standards in Washington, DC (test number 219952 dated 12/18/78). In addition, the mercury thermometer was inserted into the cardiotomy reservoir or the reservoir bag and the mercury bulb situated in the top 5 cm layer of blood. This temperature, $T_{CARD}$, when compared to $T_i$, indicated the degree of thermal mixing within in the reservoir. For the GISH system, the temperature was measured at the patient end of the administration set.

For each RC system the temperatures were measured every 30 seconds until $T_o$ reached 9-10°C. At that point the recirculation was stopped and blood flow was directed into a collecting bag which took the place of the myocardium. During this cardioplegia “administration”, $T_i$ and $T_o$ were recorded at 10, 20, 30, 45, 60, 90 and 120 seconds. This procedure was carried out for blood flows of 210, 350 and 525 ml/min.

For SP, the 3 liter bag in which the blood was collected (hematocrit adjusted to 20 percent) served as the “oxygenator blood”. For determination of cooling rate, blood maintained at 25°C served as the cardioplegia additive solution. This avoided dilution of the blood with crystalloid additive solution and allowed for repeated use of the blood while maintaining a clinically acceptable cardioplegia hematocrit. The “oxygenator

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blood" in the bag was brought to the desired temperature (37°, 31° or 25°C) utilizing the heat exchanger. The blood in the tubing of the circuit and the cardioplegia solution was 25°C. The blood cardioplegia temperatures were measured at the patient end of the tubing set using the myocardial needle temperature probe previously described. Thus, for each set of measurements the "oxygenator blood" was at a predetermined temperature, and the cardioplegia and prime were at room temperature (25°C). A blood flow rate was set to one of the values of 175, 300, 425, 525, or 667 cc/min, the ice water circulated at 4 L/min through the heat exchanger for one minute and the cardioplegia pump started. Temperatures were measured at 10, 20, 30, 45, 60, 90 and 120 seconds. For the blood flow to cardioplegia additive solution flow ratio of 1 to 1 the blood hematocrit was adjusted to 12.5 percent and the process repeated.

A submersible pump (Model NK-2) placed in a bucket filled with ice water circulated the water through the heat exchanger. For the Shiley heat exchanger, the water flow was 4 L/min. For the GISH system, the water flow was only 2 L/min.

Uniformity of Mixing

Heparinized human blood collected from the CPB circuit at the end of bypass was used to evaluate uniformity of mixing. Recirculation circuits were primed and de-bubbled with 350–400 ml crystalloid prime. Blood was then added to make the total volume 1000 ml in the bag reservoir and 1100 ml in the hardshell reservoir (GISH or cardiotomy). Recirculation was started (500 ml/min), potassium added and cooling begun. When the temperature at the outlet of the reservoir reached 9-10°C, the patient administration line was unclamped, the recirculation line clamped and infusion of cardioplegia started. Samples were taken from the infusate at the patient end after infusion of 100 ml and 900 ml of blood cardioplegia. These samples are identified as "beginning" and "end" of infusion. The samples were analyzed for hematocrit and potassium ion (K⁺) concentrations. (Nova model 1). The Journal of Extra-Corporeal Technology

Perfusion Pressure

The perfusion pressure was measured at the outlet of the roller pump. A pressure transducer, (Bentley Transrtec #800) and pressure monitor (Datascope #870) were used for pressures up to 300 mmHg. For higher pressures, a Weiss Compound gauge with a pressure isolator (Model THP B18-2) was used. The pressure transducer and pressure isolator were placed at the same level as the cardioplegia patient infusion port. Blood with a hematocrit of 15 percent and a temperature of 10°C was pumped at 300 or 500 ml/min. The pressure was measured during recirculation and during infusion. For the infusion measurements, neither cannula nor catheter were employed, the recorded pressures were due only to the lines and their associated connectors.

Ease of Use

Ease of use was evaluated by comparing the setup required for initial and subsequent infusions, priming, limitations, advantages and temperature control.

Figure 2: Temperature decrease with time for recirculation with a cardiotomy used as a reservoir.
Results

The rate of decrease in blood cardioplegia temperature for RC-CARD system at a recirculation rate of 525 ml/min is shown in Figure 2. The temperature at the outlet of the heat exchanger, $T_o$, reached 10°C in 3½ minutes. The heat exchanger inlet temperature, the outlet of the cardiomyotomy reservoir, $T_i$, reached 10°C in seven minutes. When $T_o$ reached 10°C, $T_i$ was 16°C. When $T_i$ reached 10°C, $T_{CARD}$ was 6°C. The temperature of the top blood layer in the reservoir, $T_{CARD'}$, stayed 10°C to 15°C above $T_i$. This temperature difference between the top and bottom of the reservoir was seen only for the initial infusion. When the cardioplegia was infused to the patient, $T_i$ started at 9.5°C but as the reservoir emptied and the warmer top layers of blood were pumped, $T_i$ rose to 14°C.

The $T_i$ and $T_o$ measured for RC-Bag were similar to those found for RC-CARD, however, the temperature at the top layer was the same as $T_i$. With the GISH system, it took twice as long for $T_o$ to reach 10°C than with the other two RC systems. For RC-Bag or the GISH system, when $T_i$ reached about 10°C and the blood was infused to the “patient,” $T_i$ remained stable within ±0.5°C.

At low flow rates (210 ml/min) using RC-CARD and RC-Bag, more than 10 minutes were required for $T_i$ to reach 10°C. However, $T_o$ reached 10°C in less than 20 seconds. At this low blood flow, the difference between $T_i$ and $T_o$ increased so that when $T_i$ = 36°C, $T_o$ = 10°C and when $T_i$ = 11.6°C, $T_o$ = 3.6°C. At flows of 350 ml/min, 3.8 minutes were required to obtain a $T_o$ of 10°C. When $T_o$ = 10°C, $T_i$ was 17.3°C and $T_{CARD}$ was 34.4°C.

The cardioplegia infusion temperature ($T_{inf}$) obtained for SP with a blood to crystalloid ratio of 4:1 at different flows and inlet oxygenator temperatures are shown in Figure 3. To obtain an infusion temperature of 10°C the maximum blood flows were 230 ml/min for an oxygenator temperature ($T_{oxy}$) of 37°C, 335 ml/min for $T_{oxy}$ of 31°C and 425 ml/min with a $T_{oxy}$ of 25°C. The rate of change of blood flow as a function of infusion temperature at $T_{inf}$ = 10°C for $T_{oxy}$ = 37°C, 31°C and 25°C were 48, 59 and 65 (ml/min)/°C respectively. Decreasing the ratio of blood to crystalloid from 4:1 to 1:1 at $T_{oxy}$ = 37°C shifted the curve of the $T_{inf}$ versus blood flow to the right where it corresponds to the curve obtained for a 4:1 ratio with $T_{oxy}$ = 31°C. Thus, at the lower ratio the blood flow could be increased from 235 to 340 ml/min and maintain the same $T_{inf}$ of 10°C.

It was noted that the 4:1 blood to crystalloid ratio tubing, when measured by filling volume or calculated from the tube dimensions, resulted in a ratio of 4.5:1.

Uniformity of Mixing

The results obtained for the hematocrit taken at the beginning of cardioplegia infusion ($Hct_i$) and towards the end of infusion ($Hct_f$) are shown in Figure 4. For RC-CARD primed with crystalloid for the first infusion $Hct_i$.
was only 64 ± 3.1 percent of Hct, Hct, was not different than Hct for subsequent infusions with RC-CARD or for any of the infusions with the other cardioplegia delivery systems.

Similar results were obtained for potassium measured at the beginning [K+]b, and towards the end of infusion [K+]. The only differences between [K+]b, and [K+]b were seen for the first infusion with RC-CARD when [K+] was 19 ± 3.7 percent higher than [K+].

Perfusion Pressure

The perfusion pressure for RC-CARD or RC-Bag during recirculation was 100 mmHg at 300 ml/min and 150 mmHg at 500 ml/min. This compares to 400 mmHg and 800 mmHg respectively for the GISH system. When the blood cardioplegia was infused into the patient at 300 or 500 ml/min, the perfusion pressures were 40 and 90 mmHg respectively for all systems except the GISH. For the GISH system the perfusion pressures at 300 and 500 ml/min were 220 mmHg and 460 mmHg respectively.

Priming Volume

The priming volume was the volume required to fill the tubing and heat exchanger. For RC-CARD and GISH an additional 200 ml of solution were allowed to cover the exit port. This is required by the manufacturer of GISH and is safer for RC-CARD as it will prevent sucking of air due to vortex formation at high infusion flows. The priming volumes obtained were: GISH 350 ml, RC-CARD 450 ml, RC-Bag 200 ml and SP 200 ml.

Discussion

Evaluation of the four cardioplegia delivery systems showed significant differences between RC and SP, between the two different RC circuits and between the RC circuits that were identical except for the reservoirs used. Ideally, a blood cardioplegia delivery system should instantaneously provide a homogenous solution with a desired concentration of cardioplegia components and temperature. It should have a low prime volume, require a low perfusion pressure, and be easy to operate. None of the systems tested met all of these criteria.

For recirculating systems the time required to obtain an infusion temperature of 10°C depends on the inlet temperature, blood flow, water flow, water temperature, heat exchanger performance factor and the volume of cardioplegia to be cooled. For any specific set up the only variables are blood volume to be cooled, its initial temperature and the flow rates. For RC-CARD and RC-Bag all the cited factors were identical except for the reservoir. With either reservoir it was shown that a 10°C infusion temperature can be reached in almost one half the time if the infusate is taken after the heat exchanger instead of before the heat exchanger. Using the blood before the heat exchanger to infuse to the patient at a T = 10°C results in a T much less than 10°C. Since the probability of activating cold agglutinins increases with decreasing temperature, it is not desirable to cool the blood more than required. The differences between T and T increased as the blood flow decreased. With RC-Bag or RC-CARD, T corresponds to single pass delivery system with T being equivalent to the oxygenator temperature. From the data collected for SP, it was found that for each T there was a corresponding blood flow that resulted in a T of 10°C. Therefore, for RC-Bag or RC-CARD the blood cardioplegia volume should be cooled at high recirculation to provide a T that will give a T of 10°C at the desired infusion rate. Once that T is reached the cooling can cease. This procedure will produce a uniform infusion temperature without exposing the blood to excessively low temperatures.

Recirculation has the advantage of providing a pre-mixed and pre-cooled blood volume ready for infusion at a temperature that is easy to control. The RC-CARD has the advantage of providing an easy to read, easy to set up reservoir with gentle flow conditions and a pre-pump filter. The possibility of micro air emboli is very low. Its disadvantage is that a large volume must be taken out of the cardiopulmonary bypass circuit requiring larger prime volumes. In addition, it provides poor mixing when a cardiotomy reservoir primed with crystalloid is used. The poor mixing with RC-CARD was shown by differences in hematocrit, [K+] and temperature between samples taken at the beginning and the end of the first infusion. The lack of mixing was due to blood gently flowing through the filter to the bottom of the cardiotomy reservoir and displacing the crystalloid prime solution to the top.

For all the RC systems, concentration of the cardioplegia components in the prime or residual circuit volume must be accounted for when cardioplegia components are added for the next infusion. For example, if 500 ml of blood with [K+] of 30 mEq/L are left in the reservoir and circuit from the first infusion and the second infusion requires only 15 mEq/L of [K+], then the reservoir must be emptied into the oxygenator and refilled with low [K+] blood (see "Ease of Use" below). When the RC systems are primed with crystalloid the
first infusion of blood can have a very low hematocrit. A 400 ml crystalloid prime for a total of 1000 ml blood cardioplegia solution reduces the hematocrit of the blood collected from the oxygenator by 40 percent.

RC-Bag provided better mixing of blood and its additives. This is due to flow conditions as well as the ability to mix by squeezing the bag. The RC-Bag is also inherently safer in preventing air embolism due to accidental emptying of the reservoir but does have a maximum cardioplegia delivery volume of 1000 ml.

The GISH delivery system provides a compact RC system. GISH cooling rates were slower than the other RC systems. This was partially due to the lower flow of ice water caused by the high resistance in the connectors of the heat exchanger. Mixing was very good. The GISH system’s resistance to blood flow in the connectors and recirculation tubing, although acceptable for crystalloid, is high for blood. The perfusion pressure for infusion was about 50 percent lower than for recirculation indicating that the resistance was mostly due to the small ID (1/8") long infusion/recirculation line. Replacing this tube with 3/16" ID tubing should reduce the resistance significantly.

The Buckberg-Shiley single pass system was found to be blood flow limited. The maximum blood flow that provided 10°C infused cardioplegia temperature depended on the combination of the oxygenator blood temperature and the blood to crystalloid ratio. The higher the oxygenator blood temperature the lower the cardioplegia flow that could be used and still provide $T_{inf} = 10°C$. Reduction in the ratio of blood to crystalloid provided more room temperature crystalloid which lowered the mean inlet temperature of the blood-crystalloid mixture from 35 to 31°C allowing higher maximum flow. This maneuver is most effective when $T_{oxy}$ is much greater than $T_{crystalloid}$ and should be used only if the lower hematocrit associated with the lower ratio is acceptable. Circulating ice water through the heat exchanger before beginning cardioplegia administration provided a lower temperature for the first 150 ml in the heat exchanger. However, this temperature is not controlled and it is lower than 10°C. If infusate temperatures higher than 10°C are acceptable then the blood flow rate can increase significantly. An increase from 230 ml/min to 330 ml/min can be achieved with $T_{oxy} = 37°C$ when a $T_{inf} = 12°C$ is acceptable instead of 10°C.

The advantages of the single pass system are: very good mixture of blood and cardioplegia components, excellent control of final additive concentration, simple to set up, low prime volume, avoids removal of large blood volumes from the CPB circuit and provides cold cardioplegia on demand. Its disadvantages are that the outlet temperature is not easily controlled, the crystalloid prime or any other cardioplegia solution must be cleared before a solution with different component concentration can be infused and the maximum flow that can be infused is limited by the presently used heat exchanger. The maximum flow can be increased by using either lower $T_{oxy}$ or using a heat exchanger with greater heat exchange capacity. While outlet temperature can be controlled by adjusting blood flow or oxygenator temperature, the latter may not be practical and the former should be adjustable to the patient’s requirements.

With single pass, for any blood to crystalloid ratio, the infusate temperature, $T_{inf}$, is dependent on the blood flow and oxygenator temperature, $T_{oxy}$. For any given $T_{oxy}$, $T_{inf}$ depends directly on the blood flow. The degree of dependency can be expressed by the slope of the curves describing $T_{inf}$ versus blood cardioplegia flow (Figure 3). Thus, for each 1°C increase in desired $T_{inf}$ from 10°C the blood flow can be increased by 48, 59 and 65 ml/min when $T_{oxy}$ is 37°C, 31°C and 25°C respectively. The values indicate that relatively large changes in flows will cause small changes in $T_{inf}$. Similarly, an increase in $T_{oxy}$ of 6°C would increase $T_{inf}$ by only 1.5°C. Though $T_{inf}$ does depend on blood flow and $T_{oxy}$, it is manageable within the clinical settings.

The hematocrit of blood cardioplegia, $Hct_c$ with single pass depends on the hematocrit in the oxygenator ($Hct_{oxy}$) and the blood to crystalloid ratio used.

$$Hct_c = Hct_{oxy} \times \frac{B}{B + C}$$

where $B$ is the blood portion of the B:C ratio
$C$ is the crystalloid portion of the ratio

For a 4:1 ratio, $Hct_c = 0.8 \times Hct_{oxy}$ and for a 1:1 ratio, $Hct_c = 0.5 \times Hct_{oxy}$.

Ease of Use

The single pass system was the easiest to set up, required the lowest prime volume, least tubing and provided easy predictable cardioplegia component concentration. A desired change in the concentration of cardioplegia components did require changing of a premixed crystalloid bag.

The heat exchanger incorporated in the reservoir made the GISH system the second easiest system to set up. Furthermore, the GISH system required less priming volume and tubing than either RC-CARD or RC-Bag. RC-CARD required the greatest priming volume, the additional volume corresponding to that held up by the sponge of the cardiotomy and its associated filter. All RC systems require calculations to determine the amount of cardioplegia components to be added. The
additives are a function of the desired final concentration \( (C_f) \), the concentration \( (C_i) \) and volume \( (V_i) \) of the blood added and the initial concentration \( (C) \) and volume \( (V) \) in the cardioplegia set up.

\[
\text{Addition} = C_f x (V_i + V_j) - (C x V_i + C x V_j)
\]

**Conclusion**

All four cardioplegia delivery systems evaluated were acceptable for clinical use. Each had its advantages and disadvantages. The choice of a system depends on clinical setting. If single pass can deliver cardioplegia at the desired infusion temperature then it should be used. If it does not, then a recirculation delivery system, preferably with a heat exchanger incorporated in the reservoir with low resistance recirculation lines is the second choice. If a cardiomyotomy reservoir is used, one must be aware of the poor mixing occurring when blood is added to crystalloid prime.

**References**