

Is the Air Handling Capability of the Quadrox D Pump Dependent within an ECMO Circuit? An In Vitro Study

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Abstract: The occurrence of gaseous microemboli (GME) within the extracorporeal membrane oxygenation circuit is largely overlooked, as are methods to ameliorate this occurrence. We aimed to determine if the air handling capability of the Quadrox D oxygenator was dependent upon whether it was used in conjunction with a centrifugal or roller pump; and if application of a Pall air eliminating filter (AEF) would prevent circuit air introduction from intravenous infusions. Using a blood primed circuit 1 mL of air was infused pre pump. GME were quantified post pump and post oxygenator using the EDAC[®] Quantifier. Trials were conducted at 1 and 2 L/min flow. To prevent GME recirculation a Capiox SX18 was used in circuit with negative pressure applied to its oxygenator; an EDAC[®] cuvette distal to this device quantified GME recirculation. Following air infusion, 3–5 minute data recordings were carried out for each trial. Separate trials were carried out for

centrifugal and roller pumps, and for each flow rate. The process was then repeated following the application of the AEF to the air infusion line. More GME were detected post Quadrox D when the centrifugal pump was used in comparison to the roller pump at 1 L/min ($p \leq .05$), and 2 L/min ($p = .05$). A greater volume of air was detected post Quadrox D when used in conjunction with the centrifugal device at 1 L/min ($p \leq .05$), and 2 L/min ($p \leq .05$). Application of the AEF resulted in zero GME detected at any circuit location. The results of this study confirm that a greater total count and volume of GME are detected distal to the Quadrox D when used in conjunction with a Rotaflo centrifugal pump. Application of a Pall AEF to infusion and drug lines can prevent air introduction from this source. **Keywords:** gaseous microemboli, oxygenator, centrifugal pump, roller pump, extracorporeal membrane oxygenation, EDAC[®]. *JECT. 2010;42:203–211*

The occurrence of gaseous microemboli (GME) within the cardiopulmonary bypass (CPB) circuit has been repeatedly documented within the perfusion, anaesthesiology, and cardiothoracic surgical literature. Commonly reported sources of GME during CPB procedures include drug administration into the venous side of the CPB circuit (1–3), the use of integral cardiotomy reservoirs (4), the application of vacuum assisted venous drainage (VAVD) (5,6), and air entrainment from around the venous cannulae (2).

Many methods for reducing the occurrence of GME within the CPB circuit have been suggested over recent years. Commonly recommended methods are the circulation

of the CPB prime through a .2 micron pre-bypass filter (7), the removal of air from drug syringes used to administer medication into the venous line manifold (1), the use of arterial line filters (4,6), and the prevention of air entrainment into the venous line (8). Suggested methods to completely eradicate CPB related air are the employment of off pump procedures (9).

Little doubt exists over the presence of GME within the CPB circuit. Contention does however arise when the clinical effects of GME upon the patient are discussed. Many authors report a link between the counts of cerebral microemboli delivered to the patient and postoperative cognitive dysfunction (POCD) (1,10). Other studies, however, find no association between the amount of microemboli detected and the degree of POCD (9).

While the debate about the effects of GME continues, researchers and clinicians continue to strive to minimize the occurrence of GME within the extracorporeal circuit and ultimately the subsequent transmission to the patient. One particular area of extracorporeal support where the occurrence of GME is frequently overlooked is

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extracorporeal membrane oxygenation (ECMO). ECMO is a therapy that is offered to patients always after the failure of standard medical and surgical options. The possibility exists that this therapy may be complicit in poor patient neurological outcomes partly through the impact of GME. Possible reasons for the oversight of GME for the ECMO patient may include the lack of many of the interfering factors outlined above occurring during ECMO; another reason may be the reduced perfusionist input into a therapy gradually becoming part of the intensive care domain.

Nevertheless, the ECMO circuit remains a form of CPB circuit with venous line, blood pump, oxygenator, and arterial return line. What this circuit invariably lacks is a reservoir and an arterial line filter, two features which have been repeatedly linked to a reduction in GME. Certainly the arterial line filter is widely viewed as the single most important feature of an extracorporeal circuit in the prevention of GME return to the patient (11).

It is important to remember that the ECMO patient often has multiple continuous intravenous infusions, still requires boluses of drugs, crystalloid fluids, and blood products all of which take place over a prolonged period of time. Venoarterial ECMO is in essence a built in right to left shunt. The significance of a right to left shunt within this setting is that any air introduced into the venous system, if not removed, may be returned to the systemic arterial circulation by way of the ECMO circuit.

Within the clinical setting we observed a gradual build up of air around the connector joining the venous cannula to the venous return line on several neonatal ECMO patients. This collection increased in size rapidly following bolus administration of medication or fluids. At times the collection of air would travel into the centrifugal pump head (our standard pump choice) and then be delivered to the oxygenator appearing greatly reduced in size. No visible air was ever witnessed distal to the oxygenator. A Medtronic air detector (Medtronic, Minneapolis, MN) was situated distal to the Quadrox D, which did not detect any bubbles. These devices have a $>.5$ mL detection capability. It is important to acknowledge that the ECMO circuit used clinically did not include any form of bladder or venous reservoir.

The primary hypothesis of this study was that the air handling capability of the Quadrox D oxygenator (Maquet Cardiopulmonary AG, Hirrlingen, Germany) was dependent upon whether it was used in conjunction with a centrifugal pump (Rotaflow, Maquet Cardiopulmonary AG, Hirrlingen, Germany) or a roller pump (Cobe Cardiovascular, Arvada, CO). The secondary hypothesis was that the application of a Pall Supor .2 μ m Air Eliminating Filter (Pall Medical, Port Washington, NY) would prevent extracorporeal circuit air introduction from intravenous infusions.

MATERIALS AND METHODS

Circuit Design

The simulated ECMO circuit used in this study was set up to represent our standard ECMO circuit plus inclusions to facilitate the experiment (Figure 1). The venous line consisted of polyvinyl chloride (PVC) $3/8" \times 3/32"$ tubing. This was attached to the particular pump under investigation, either the Jostra Rotaflow centrifugal pump or the Cobe roller pump containing a $3/8" \times 3/32"$ raceway. Specific to the roller pump the occlusion was set to be just occlusive. The pump was connected to the Quadrox D oxygenator with $3/8" \times 3/32"$ tubing. This length of tubing included a Medtronic Bio Probe flow transducer (Medtronic, Minneapolis, MN), which was used to measure blood flow for all trials. For all experimental trials the deairing cap of the Quadrox D was removed. The arterial return line exiting the Quadrox D consisted of PVC $3/8" \times 3/32"$ tubing. To facilitate de-airing of the circuit, and to reduce the recirculation of GME, the arterial return line was connected to the oxygenator and then reservoir of a Capiiox SX18 (Terumo Corporation, Tokyo, Japan). To further enhance the prevention of GME recirculation the Capiiox SX18 oxygenator was placed under a negative pressure of negative 525 mmHg by the application of a suction device to the "gas in" port, and the sealing of the "gas out" and emergency relief port. To infuse air into the circuit a 100 cm infusion line was attached to the venous line approximately 75 cm pre blood pump. The pump used to infuse the air was a Graseby 3200 infusion pump (Smiths Medical, Kent, UK), via a $3/8" \times 3/8"$ luer connector. The pump was set to administer 1 mL of air over 10 seconds. The circuit contained three microemboli detection/quantification cuvettes (EDAC[®], Luna Innovations, Inc., Blacksburg, VA). EDAC[®] cuvette one was placed immediately distal to the Capiiox SX18 reservoir and oxygenator, proximal to the air infusion

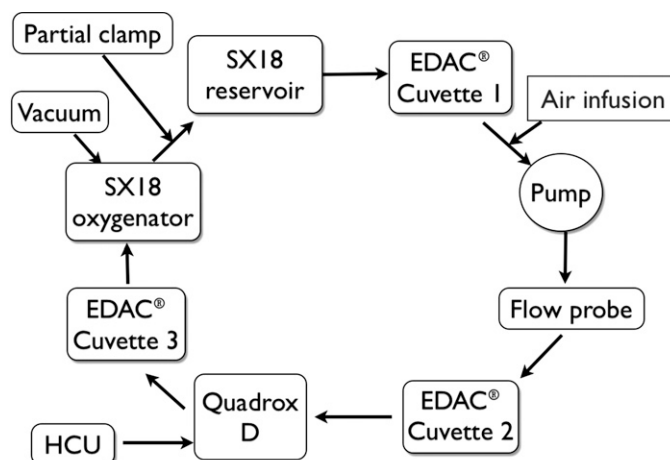


Figure 1. Schematic diagram representing the experimental circuit. HCU, Heater Cooler Unit.

pump, approximately 100 cm pre blood pump. The purpose of this cuvette was to assess for recirculation of GME that were not removed by stated preventative measures. EDAC[®] cuvette two was placed 30 cm post pump. The purpose of this cuvette was to assess the degree of microemboli generated by each particular pump. EDAC[®] cuvette three was placed 30 cm post Quadrox D. The purpose of this particular cuvette was to quantify the microemboli that pass through the Quadrox D. All EDAC[®] cuvettes were attached to the EDAC[®] Quantifier (Luna Innovations, Inc., Blacksburg, VA). Due to the presence of an open reservoir, no bladder box was required or included with the experimental set up. The circuit was primed with Plasma-Lyte 148 (Baxter Healthcare, Toongabbie, Australia), 100 mL of 20% albumin (Albumex 20, CSL Bioplasma, Broadmeadows, Australia), and packed red blood cells resulting in a hematocrit (Hct) of 26%. To enhance the effects of buoyancy on de-airing, the Capiiox SX18 reservoir level was maintained at 600 mL. To eliminate blood temperature as a variable a circuit temperature of 36.4°C was maintained by the use of a true heater cooler unit, the Cincinnati Subzero (CSZ, Cincinnati, OH) attached to the Quadrox D. A partial clamp was placed immediately proximal to the Capiiox SX18 device to generate a circuit pressure of 150 mmHg. Based upon clinical practice for the flow rates being tested, a gas flow of .5 L/min was run continuously into the Quadrox D. To prevent the introduction of gas gradients that may affect GME absorption, air was utilized as the chosen gas. When assessing if air introduction into the circuit could be prevented the same process as outlined was followed with the addition of a Pall AEF to the distal end of the air infusion line.

EDAC[®] Quantifier

The EDAC[®] quantifier utilizes ultrasound technology in the detection of GME within the extracorporeal circuit. The information gained by the device is translated into real time data pertaining to microemboli size, volume, and total count. This process can be carried out at three separate circuit locations simultaneously. Microemboli within the size range of 10 μm –12,700 μm can be detected, and at rates up to 1000 emboli per second. The recommended flow rates for which this device optimally performs are .2 L/min and 6.0 L/min.

Experimental Design

Ethics approval was obtained on October 1, 2009 for the use of the de-identified human packed red blood cells used to prime the circuit. The circuit design was initially validated for the prevention of GME recirculation. This was done by the infusion of 1 mL of air into the crystalloid primed circuit. Centrifugal and then roller flow rate was 3 L per min. EDAC[®] cuvette 1, proximal to the air infusion line, was recorded for 3 minutes pre and post air insertion. Continuous visual inspection of arterial return line, distal

to the Quadrox D, was carried out to assess for visible air passing through the device. This process was repeated six times. With a blood primed circuit trials were carried out using both centrifugal and roller pump at both 1 and 2 L/min. At 1 L/min trials were carried out five times for each pump on two identical circuits. At 2 L/min trials were carried out three times for each pump on one circuit. With both pumps and at both specified speeds the experiment was repeated following the application of a Pall AEF on the air infusion line. Prior to each trial data was recorded for 3 minutes prior to air insertion and 5 minutes post air insertion, apart from the roller pump at 1 L/min where data was recorded for 3 minutes post air introduction.

Statistics

Computerized statistical analysis was performed using SPSS version 17 (SPSS, Inc., Chicago, IL) for Windows (Microsoft Corporation, Redmond, WA). Due to non-parametric analysis being appropriate for this data all results are expressed as median and interquartile range (IQR). Comparisons between paired groups were derived using the Wilcoxon signed ranks test. Comparisons between independent groups were carried out using a two sample Mann-Whitney test. A *p*-value of equal to or less than .05 was considered statistically significant.

RESULTS

Prior to the commencement of each experimental trial the circuit was assessed to be at a steady state. A small amount of circulating GME was detected at baseline, immediately pre air infusion line, .5 (IQR 0, 1). No air was ever visualized distal to the Quadrox D. Statistical analysis demonstrated no significant difference between the two identical circuits used in the 1 L/min experiment.

In all experimental trials a post oxygenator pressure of 150 mmHg was maintained. Throughout all trials at both 1 and 2 L/min using the centrifugal pump the pump inlet pressure recorded was 11 mmHg. The inlet pressure recorded when the roller pump was used, at both flow rates, was 13 mmHg. The pressure immediately pre oxygenator was not measured.

Total Count

Figure 2 shows the median number of GME detected immediately post pump and post Quadrox D. At 1 L/min there was a significant increase in the total GME count post oxygenator when compared to the post pump value for the centrifugal pump ($p \leq .05$), and a significant decrease for the roller pump ($p \leq .05$). At 2 L/min no significant difference could be found between post pump and post oxygenator values for either pump. When comparing the centrifugal and roller pump it was demonstrated that the centrifugal pump generates significantly more GME than

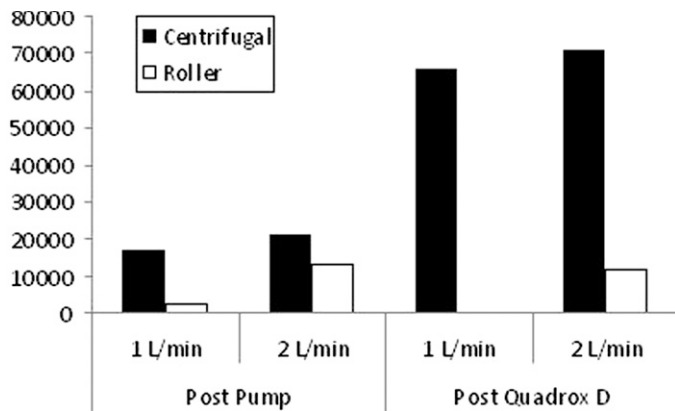


Figure 2. A comparison of post pump and post Quadrox D total median microemboli count for each pump and flow speed.

the roller pump at 1 L/min ($p \leq .05$), but at 2 L/min significance could not be demonstrated. The centrifugal pump transfers significantly more GME through the Quadrox D at 1 L/min ($p \leq .05$) and at 2 L/min ($p = .05$) than the roller pump.

When establishing the effect of flow rate upon total GME count (Figure 2), with the centrifugal pump at either 1 or 2 L/min, no significant difference could be shown between post pump counts or post oxygenator counts. When roller pump values were compared it was shown that at 2 L/min significantly more microemboli were detected post pump ($p < .05$), and post oxygenator ($p \leq .05$) in comparison to 1 L/min.

Volume

Despite 1 mL of air being infused into the circuit, 1 mL of air was never recorded pre oxygenator. When post pump volumes are compared (Table 1) significantly less air was actually delivered to the Quadrox D when used in conjunction with centrifugal device at 1 L/min ($p \leq .05$). Significance could not be demonstrated for the same comparison at 2 L/min. Despite a smaller volume of air being delivered to the Quadrox D when used in conjunction with the centrifugal device a significantly larger volume was recorded post Quadrox D when used in conjunction with the centrifugal device at 1 L/min ($p \leq .05$) and at 2 L/min ($p \leq .05$).

Size

When post pump and post Quadrox D values are compared (Tables 2 and 3) at 1 L/min using the centrifugal pump, significantly more GME are detected post Quadrox D in the size range $<40 \mu\text{m}$ ($p \leq .05$), and $40\text{--}100 \mu\text{m}$ ($p \leq .05$); decreases are seen in the size range $100\text{--}200 \mu\text{m}$ ($p = .05$) and $>200 \mu\text{m}$ ($p \leq .05$). The roller pump at 1 L/min recorded significantly less GME post Quadrox D across all size ranges ($p \leq .05$). The centrifugal pump generated significantly more GME post oxygenator, across all size ranges, at 1 L/min ($p \leq .05$) and at 2 L/min ($p \leq .05$) in comparison to the roller pump.

When determining the effect of the different flow rate on the size of microemboli post pump (Table 2), in conjunction with the centrifugal pump, no significant difference could be found across all size ranges. Post Quadrox D (Table 3), at 2 L/min, significantly more GME were detected $<40 \mu\text{m}$ ($p \leq .05$), significantly less $40\text{--}100 \mu\text{m}$ ($p \leq .05$), with no significance in the remaining size ranges. In contrast, with the increase in flow rate, the roller pump resulted in significantly more GME across all size ranges, both post pump and post oxygenator ($p \leq .05$). The size distribution of the recorded GME, in $10 \mu\text{m}$ intervals, can be compared graphically in Figures 3–6.

DISCUSSION

GME entrained into the venous side of a CPB circuit have been repeatedly shown to pass through the reservoir, oxygenator, and arterial line filter (2,3) and then subsequently be transferred to the patient. Commonly used ECMO circuits do not generally include features such as reservoir and arterial line filter, both of which have been reported to be complicit in the reduction of GME transmission (3). Due to the ECMO patient often requiring multiple continuous infusions, and bolus administration of drugs and fluids, the issue of air introduction into this extracorporeal circuit must not be overlooked.

A tentative link has already been made between the length of CPB and the amount of microemboli the patient is exposed to (12). Post cardiectomy ECMO runs can last up to 5–7 days, admittedly lacking many of the practices linked to CPB related GME such as the use of integral

Table 1. Median (IQR) volume detected post pump, post oxygenator and volume difference following 1 mL circuit air administration.

Pump Flow (L/min)	Pump	Volume		
		Post Pump (mL)	Post Oxygenator (mL)	Difference (%)
		Median (IQR)	Median (IQR)	Median (IQR)
1	Centrifugal	.056 (.029, .066)	.004 (.003, .007)	93.354 (88.077, 94.275)
	Roller	.346 (.244, .422)	.000 (.000, .000)	99.999 (99.999, 100.000)
2	Centrifugal	.072 (.072, .080)	.002 (.002, .003)	96.966 (96.713, 97.478)
	Roller	.263 (.171, .367)	.000 (.000, .000)	99.910 (99.712, 99.951)

Table 2. Median (IQR) total microemboli count, in size ranges, post pump following air administration.

Pump Flow (L/min)	Pump	Post Pump			
		Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)
		<40 μm	40–100 μm	100–200 μm	>200 μm
1	Centrifugal	7243 (5681, 7868)	4137 (3352, 6133)	2967 (1931, 3661)	2291 (1478, 2701)
	Roller	1034 (958, 1118)	459 (365, 580)	312 (191, 403)	548 (281, 803)
2	Centrifugal	11412 (7499, 14536)	4222 (3596, 4624)	2729 (2705, 2850)	2649 (2516, 2785)
	Roller	6042 (5755, 6227)	2973 (2864, 3212)	2017 (1796, 2118)	2084 (1597, 2383)

Median, median value of GME count.

Table 3. Median (IQR) total microemboli count, in size ranges, post Quadrox D following air administration.

Pump Flow (L/min)	Pump	Post Quadrox D			
		Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)
		<40 μm	40–100 μm	100–200 μm	>200 μm
1	Centrifugal	47633 (46,640, 51757)	13766 (12,199, 16338)	1219 (787, 2597)	26 (11, 162)
	Roller	163 (114, 217)	15 (7, 23)	0 (0, 0)	0 (0, 0)
2	Centrifugal	57996 (57,637, 61851)	9388 (8474, 10521)	655 (474, 868)	11 (8, 15)
	Roller	10614 (8702, 11878)	1145 (932, 1340)	34 (26, 37)	1 (0, 3)

Median, median value of GME count.

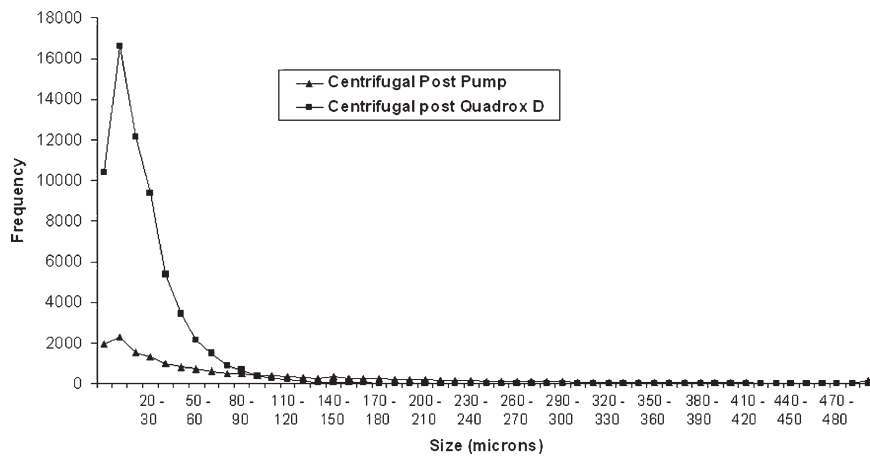


Figure 3. Frequency polygon depicting the median count of detected GME, in 10 micron intervals, post pump and post Quadrox D, following administration of 1 mL of air and when used in conjunction with a centrifugal pump at 1 L/min.

cardiotomy reservoirs (4) and VAVD (5,6) (although it could be argued that the negative pressure created by the blood pump upon the venous side of the ECMO circuit is a form of continuous VAVD); but also including one of the main features associated with circuit air introduction, namely drug administration. This drug administration may be directly or indirectly into the venous side of the extracorporeal circuit as previously reported as complicit in GME transfer to the patient (1–3).

ECMO circuits generally use either a centrifugal, or roller pump. The Quadrox D is a polymethylpentene oxygenator used in long-term extracorporeal support.

The results of this study support the primary hypothesis that the air handling capability of the Quadrox D oxygenator is dependent upon the type of pump it is used in conjunction with. The Quadrox D was shown to prevent the vast majority of the volume of received air from being transmitted to the arterial return line in conjunction with

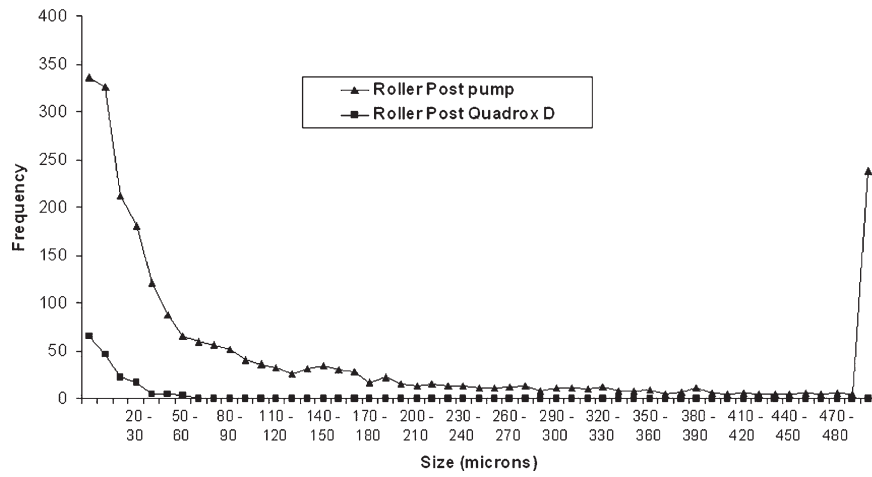


Figure 4. Frequency polygon depicting the median count of detected GME, in 10 micron intervals, post pump and post Quadrox D, following administration of 1 mL of air and when used in conjunction with a roller pump at 1 L/min.

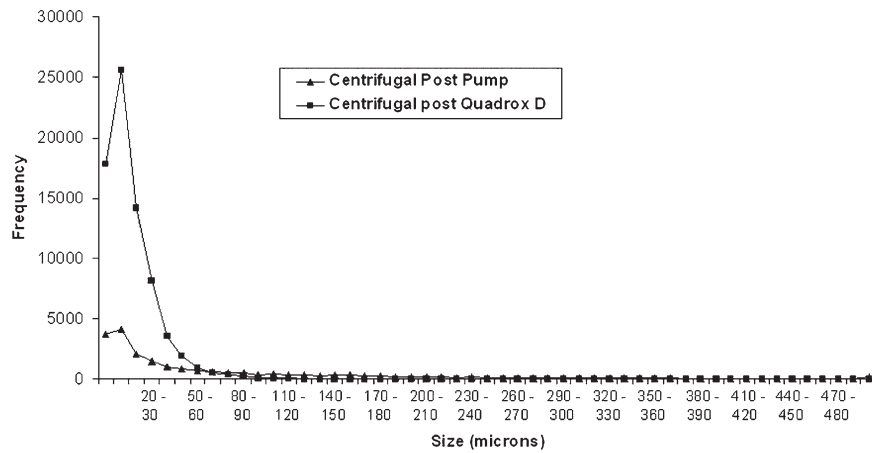


Figure 5. Frequency polygon depicting the median count of detected GME, in 10 micron intervals, post pump and post Quadrox D, following administration of 1 mL of air and when used in conjunction with a centrifugal pump at 2 L/min.

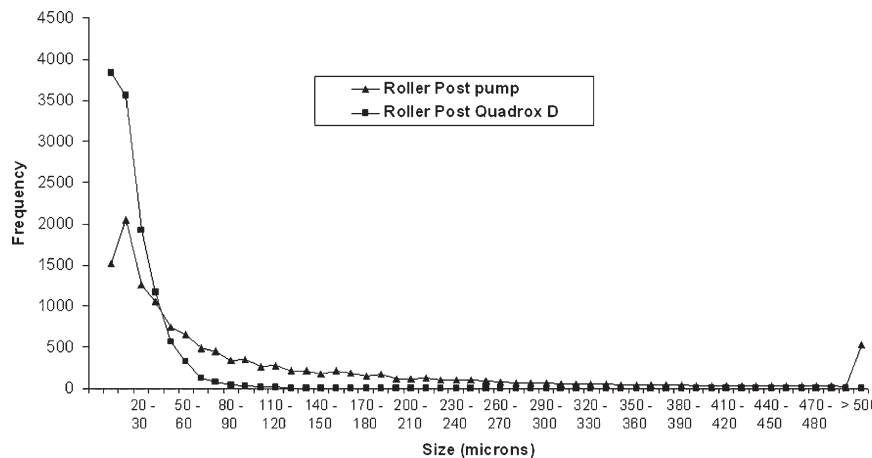


Figure 6. Frequency polygon depicting the median count of detected GME, in 10 micron intervals, post pump and post Quadrox D, following administration of 1 mL of air and when used in conjunction with a roller pump at 2 L/min.

either the roller or centrifugal pump. However, this study did demonstrate that when air was entrained into the ECMO circuit a proportion of this air will pass through the Quadrox D and be readily detected in the arterial return line regardless of which type of pump was utilized and which flow rate was used.

The volume of air actually delivered to the Quadrox D was found to be significantly different between centrifugal and roller pump. Perhaps equally noticeable was the decrease in volume post pump when compared to the 1 mL initially infused into the circuit (Table 1). This part of the circuit did contain numerous connectors and components, namely the EDAC[®] probe and associated connectors, the flow probe and associated connectors, and the Quadrox D inlet connector. During circuit deairing, following trials, numerous visible bubbles could be seen coalescing around these connectors leading one to conclude that this is a contributing factor in the volume reduction seen post pump. Specific to the centrifugal device, during the deairing procedure, numerous bubbles were removed from inside the pump head, again leading one to speculate that this may explain the significant difference in volumes post centrifugal pump when compared to the roller device.

Despite a smaller volume of air being delivered to the Quadrox D when used in conjunction with the centrifugal pump, the use of the centrifugal pump resulted in both a significantly greater volume, and greater total GME count to be detected distal to the Quadrox D in comparison to the roller pump. This difference was irrespective of the pump flow used. In fact at both 1 and 2 L/min the centrifugal pump resulted in an increase (although non-significant at 2 L/min) in GME count post Quadrox D. This finding was in contrast to the roller pump, where a reduction in count was seen post Quadrox D. However, it must be noted that at 2 L/min this reduction in GME post Quadrox D was far less obvious and failed to reach significance. This finding may lead one to speculate that at even higher flow rates the roller pump may result in an increase in GME production as seen with the centrifugal device.

If we attempt to address the reasons why a centrifugal pump not only manages to generate a significantly greater amount of GME than roller pump, but also manages to propel them through the Quadrox D to a greater extent than a roller pump, one must look at how the centrifugal pump behaves. It has been postulated that both the negative pressure applied to the air on the inlet side of a centrifugal pump, followed by the kinetic energy within the pump head, result in the generation of a large number of smaller bubbles. These smaller bubbles become suspended in the blood and therefore become increasingly likely to traverse distal circuit components (13). Smaller bubbles have been demonstrated to have greatly reduced positive buoyancy (4,14). It is this property that undoubtedly reduces the ability of such bubbles to rise to the top of the Quadrox D, and

thus be vented. This process does not however explain why, despite a reduction in GME volume from post pump to post oxygenator, the GME total count rises significantly in the post oxygenator phase when used in conjunction with a centrifugal pump.

A possible explanation as to why the centrifugal pump resulted in an increase in total count of GME post Quadrox D, when compared to post pump values, may be obtained from a recent study by Myers et al.⁴ This group discussed how when larger size bubbles are generated, within an extracorporeal circuit, they have a tendency to break up into greater amounts of smaller GME. Admittedly this study was looking at GME detected distal to an arterial filter, but this theory may be applicable to the increase in GME count post Quadrox D. What however is not clear from this study is whether the larger bubbles are generally less stable and spontaneously break up, or whether individual flow dynamics caused by circuit components are complicit in this occurrence.

In an attempt to investigate what happens to the actual bubbles attention may be drawn to the information contained within the size distribution histograms (Figures 3–6) and the numerical data contained within Tables 2 and 3. The GME size distribution data obtained from this study demonstrated that regardless of which type of pump was used, and at both tested blood flow rates, a decrease in counts distal to the Quadrox D could be seen in GME >100 μm when compared to post pump values. Therefore GME >100 μm are either trapped within the Quadrox D, vented from the Quadrox D, or become bubbles of a different size. Referring to Figures 3–6 and Tables 2 and 3, it would appear that what happens to the bubbles is pump dependent, and to a lesser extent flow rate specific.

In conjunction with the centrifugal pump it can be seen that at 1 and 2 L/min there is a significant increase in GME count <100 μm post Quadrox D. If the GME >100 μm were spontaneously breaking up, resulting in the increase in GME <100 μm , one would expect this pattern to be repeated with the roller pump. If, however, we look at the roller pump data, at 1 L/min, we can see reductions post Quadrox D across all size ranges; leading one to postulate that the larger GME are not spontaneously breaking up. We therefore believe that the predominant factor in the increase in GME across the Quadrox D is the flow dynamic created by the centrifugal pump in conjunction with the Quadrox D.

The flow dynamic created by the centrifugal pump is a continuous laminar flow, which within the Quadrox D appears to result in the breaking up of larger GME and thus contributing to an increase in smaller GME count. The roller pump flow dynamic, on the other hand, is more pulsatile in nature with periods of acceleration and deceleration. It is possible that the lower flow component, during the deceleration period, limits the forces exerted upon

the GME, thus limiting the breaking up of the bubbles within the Quadrox D. This deceleration phase would be less obvious with faster pump speeds, as witnessed when the blood flow was increased from 1–2 L/min, thus resulting in an increase in the GME count in the <40 μm size range. The caveat must be added that this theory is speculative and requires further work to be confirmed.

The results of this study also supported the secondary hypothesis, that the application of a Pall AEF would prevent air introduction from intravenous infusions into the extracorporeal circuit. This finding was independent of pump choice and flow speed. Clinically this filter can be used with continuous infusions or intermittent infusions or injections. A limitation of this device is that it can not be used with cellular fluids.

The clinical implications of these findings depend upon whether one believes that the amount, size, and volume of GME the patient is exposed to impacts upon ones POCD, detailed discussion of which is beyond the scope of this paper. It is however important to consider that assessment of any subtle cognitive deficits in the pediatric and particularly the neonatal population are, in the short term, extremely challenging. If even a possible link between the occurrence of an event and a negative outcome exists the conscientious clinician should strive to minimize its occurrence. In this instance the prevention of air introduction into the extracorporeal circuit through the application of an air eliminating filter to infusion drug lines is an effective step in this process.

The limitations of this study include the presence of an open reservoir. This study aimed to replicate a closed ECMO circuit, yet the desire to eliminate recirculation of GME led to the inclusion of an open reservoir within the circuit setup. Whilst the inclusion of an EDAC[®] cuvette distal to this device showed no significant recirculation or addition of GME, the inclusion of this device does detract from the aim of a closed ECMO circuit replication.

Further limitations include the small sample size being used for the 2 L/min trials, and this group only being studied on one circuit. The small sample size may have been complicit in the difficulty in obtaining statistical significance when inter-group analysis was applied to the 2 L/min trial. Further limitations of this study include the use of 3/8" tubing not reflecting the size of tubing commonly used with the flow rates used in this study. This choice was due to balancing an initial aim of testing a wider range of flow rates with the resources available. The authors do acknowledge that adult ECMO primarily involves flow rates greater than those tested in this study. The recirculation of GME confounded results at flow rates greater than 2 L/min leading to these experiments being abandoned with the current model. Interestingly it was observed that GME recirculation was not a confounding issue when the circuit was primed with crystalloid. It has been previously

reported that GME < 300 μm become protein coated and thus reduce their susceptibility to breaking up (3,4). It is possibly due to this fact that we encountered problems at higher flow rates in the blood primed circuit. A further limitation of this study was that the EDAC[®] only recorded for 3 minute post air infusion in the 1 L/min roller pump trial, this is in contrast to 5 minutes for all other trials. The reason for this difference was simply a rapid return to baseline values, and not a deliberate attempt to confound results.

CONCLUSION

Air introduction into the venous side of an ECMO circuit can be routinely detected distal to a Quadrox D oxygenator within the arterial return line. Use of a Rotaflo centrifugal pump results in greater counts, volume, and larger sized GME detected distal to the Quadrox D when compared to a roller pump at the blood flow rates, pressures, and Hct tested. Despite an association between GME and POCD not being definitively established, the application of a Pall AEF to infusion and drug lines will eliminate air introduction from this source and potentially limit the degree of POCD patients may encounter. Application of an EDAC[®] in the clinical setting may be a valuable adjunct to the care of the ECMO patient.

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