Original Article

Gross Air Handling Characteristics of Membrane Oxygenators: An In Vitro Study

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ABSTRACT

The goal of this study was to quantitate gross air handling characteristics of membrane oxygenators. Three oxygenator designs were tested: 1) flat plate, 2) blood-inside hollow fiber, and 3) blood-outside hollow fiber. Neither filters nor bubble traps were utilized in the test circuit; however, the purge line remained open during testing. The priming solution was Plasmalyte and expired human blood. The total circuit volume was 1000 ml with a resulting hematocrit of 23-25%. Tested blood flow range was 1-5 L/min and tested temperatures were 25°, 30° and 37°C. Tests were performed with oxygenator gas flow either on or off. Air boluses were introduced and counted by a micro bubble detector. In this study, all six oxygenators allowed macro air bubbles to pass through at flow rates of 1, 2, 3, 4 and 5 L/min. The distribution of non-visual micro bubble numbers and sizes varied with the flow rates and size of introduced air boluses. High flow rates (3-5 L/min) and 10-30 ml air boluses produced larger (81-160 μm) micro bubbles and low flow rates (1-2 L/min) and 5 ml air boluses produced smaller (1-80 μm) micro bubbles. This study shows that while membrane oxygenators may moderate, they cannot eliminate micro bubbles. Therefore, membrane oxygenators do not eliminate the risks of air during during cardiopulmonary bypass. The results suggest that arterial filters/bubble traps should be used in cardiopulmonary bypass circuits with membrane oxygenators.

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INTRODUCTION

During the past ten years membrane oxygenators have been significantly improved and widely used in cardiac surgery. Membrane oxygenators, unlike bubble oxygenators, do not have a direct blood-gas interface. Instead, they have a gas permeable membrane. Between the gas side and the blood side of the membrane, gas exchange takes place by diffusion. Their superiority is recognized by less trauma to blood formed elements when in the absence of antifoam agents (1-3). Membrane oxygenators have been shown to have almost nonexistent microemboli production under certain conditions (4,5) However, while membrane oxygenators do not generate air emboli, their ability to prevent the passage of introduced air through the blood path has not been clearly documented. The purpose of this study was to examine the ability of membrane oxygenators to prevent the passage of introduced air under a variety of conditions.

MATERIALS AND METHODS

The test circuit was constructed using commonly available equipment (Figure 1). The tubing was Tygon® medical grade polyvinyl chloride with a 3/8-inch inside diameter and 3/32-inch wall thickness. A centrifugal pump (Bio-Pump®) and a venous reservoir bag (Bentley-1900®) were used. Neither arterial filters nor bubble traps were utilized in the test circuit. The oxygenator

**Figure 1**
The in vitro test circuit employed to count micro bubbles from six membrane oxygenators.

**Figure 2**
Mean micro bubble counts of six membrane oxygenators for each size at 37°C, 5 L/min, 10 ml air, with gas flow. The micro bubble size 121-160 μm was more frequent than the sizes 1-40 μm and 41-80 μm (p<0.01).
purge lines remained open during testing. The priming solution was Plasmalyte® (pH 7.4) and expired human blood. The hematocrit was maintained at 23-25% during testing. Total circulating fluid volume was 1000 ml and temperature was maintained by utilizing a Hemotherm® cooler/heater unit. Six membrane oxygenators were tested: Shiley M2000® (flat plate); Bentley CM50® and Terumo Capiox 350® (blood-inside hollow fiber); Bentley Univox®, Medtronic Maxima® and Shiley Plexus® (blood-outside hollow fiber). Micro bubble counts were separated into size ranges by a pulse Doppler system that contained an external bubble detecting probe (Hatteland BD-100 micro bubble detector) and a digital computer (Otrona Attache Portable Computer) used for data processing. The software utilized for data processing was created in part by Extracorporeal Technologies Inc. (6,7).

The oxygenators were placed in the circuit in accordance with their specifications. The micro bubble size 121-160 μm was more frequent than the sizes 1-40 μm and 41-80 μm (p<0.001).

**Figure 3**
Mean micro bubble counts of six membrane oxygenators for each size at 37°C, 5 L/min, 30 ml air, with gas flow. The micro bubble size 121-160 μm was more frequent than the sizes 1-40 μm and 41-80 μm (p<0.001).

**Figure 4**
Mean micro bubble counts of six membrane oxygenators for each size 25°C, 3 L/min, 5 ml air, without gas flow. The micro bubble size 121-160 μm was more frequent than the size 1-40 μm (p<0.01).

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a Norton performance Plastics, Akron, OH
b Medtronic Cardiopulmonary Division, Anaheim, CA
c Baxter Healthcare Corp., Bentley Laboratories Division, Irvine, CA
d Baxter Healthcare Corp., Deerfield, IL
e Cincinnati Sub-Zero, Cincinnati, OH
f Sorin Biomedical, Irvine, CA
g Terumo Corp., Somerset, NJ
h Hatteland Instrumentering, Oslo, Norway
i Extracorporeal Technologies Inc., Indianapolis, IN
with manufacturers’ recommendations. The oxygenator outlet pressure was measured and controlled at 50±5 mmHg using a partial occlusion clamp on the oxygenator outlet side for each blood flow rate. Calibration of the BD-100 micro bubble detector incorporated the following: 40 μm filter, 2.0 V voltage cut off, 5 V signal corresponds to ~200 μm bubble. The BD-100 micro bubble detector probe was attached to the outlet of each oxygenator and had a continuous sample time of 30 seconds. Tested circulating blood flow range was 1-5 L/min and the temperatures tested were 25°, 30° and 37°C. Tests were performed with oxygenator gas flow either on or off (FiO₂ 70%). Air boluses of 5, 10, 20 and 30 ml were introduced into the blood inlet side of the oxygenators by syringe injection. After each 30-second counting period, the tested oxygenator was subjected to recirculation and debubbling until bubbles were undetectable for at least one minute. Then the next test was begun. Both visual and non-visual bubbles were detected and counted by the BD-100 and computer system for a period of 30 seconds immediately after the introduction of an air bolus. Each trial was repeated three times. All data were subjected to statistical analysis. Unpaired Students’ T-test was used to compare the differences between bubble counts of each size. Values are reported as mean ± standard deviation.

Figure 5
Mean micro bubble counts of six membrane oxygenators for each size at 25°C, 2 L/min, 5 ml air, without gas flow. The micro bubble size 1-40 μm was more frequent than the sizes 121-160 μm (p<0.01).

Figure 6
Mean micro bubble counts of six membrane oxygenators for each size at 37°C, 1 L/min, 10 ml air, with gas flow. The micro bubble size 1-40 μm and more frequent than the size 121-160 μm (p<0.01).
RESULTS

All six oxygenators allowed visible macro air bubbles to pass through the blood outlet when injected with 5, 10, 20 or 30 ml air boluses at blood flow rates of 1, 2, 3, 4 and 5 L/min, regardless of whether the oxygenator gas flow was on or off.

In all six oxygenators, the non-visual micro bubble counts and sizes varied in relation to the blood flow rates. When the tested blood flow rates were 3-5 L/min and air boluses were 5, 10, 20 or 30 ml, the micro bubble counts of sizes 81-120 and 121-160 μm were more frequent that the sizes 1-40 and 41-80 μm (p<0.01) (Figures 2-4). Conversely, when blood flow rates were 1 or 2 L/min, the micro bubble counts of sizes 1-40 and 41-80 μm were more frequent than the sizes 81-120 and 121-160 μm (p<0.01) (Figures 5, 6). Particularly at the flow rate of 1 L/min, the micro bubble counts of sizes 81-120 and 121-160 μm were much less frequent than the size of 1-40 μm (p<0.005).

In this study, there was little difference in number or size of the micro bubbles with regard to the temperature of the tested solution or whether the oxygenator gas flow was on or off (p>0.05) (Figures 7-9).

DISCUSSION

In clinical cardiopulmonary bypass practice, the primary concern of the perfusionist is safety and patient well-being. Many
kinds of microemboli are known to contribute to increased morbidity and mortality during open heart surgery with cardiopulmonary bypass (8). Theoretically, membrane oxygenators—unlike bubble oxygenators—do not have a direct blood-gas interface and do not need defoaming agents. Oxygen transfer occurs across a permeable membrane from gas side to blood side by diffusion (89). They have almost nonexistent microemboli in a closed circuit during cardiopulmonary bypass (4,5,10,11). It is therefore thought that membrane oxygenators are safer and may even act as a bubble trap under certain conditions (11). In the clinical circuit, the membrane oxygenator is positioned beyond the outlet of the arterial pump head and performs its functions under positive pressure conditions. In this study, macro bubbles and visual size micro bubbles tended to pass through the oxygenator outlet purge-line over an extended time in all six tested membrane oxygenators after an air bolus was introduced. Thus, an essential design of membrane oxygenators is to allow venting of air bubbles. Unfortunately, the results of non-visual size micro bubbles counted by the BD-100 showed that there were multiple-size micro bubbles exiting through the outlet side of the oxygenators when an air bolus was introduced. The micro bubble size and number varied in relation to the blood flow rates. With higher flow rates, there were more large non-visual size (81-160 μm) micro bubbles. It appears that this situation must be considered a standard risk of perfusion. Microemboli larger than 40 μm entering the patient’s circulating system may cause vital organ dysfunction (12,13). According to the oxygenating principle of membrane oxygenators, the force of gas transfer across a permeable membrane is dependent on driving pressure (11) (the difference in the pressures of a specific gas on either side of the membrane). When an air bolus was introduced into the perfusate, the resulting blood-phase gas pressure was equal to atmospheric pressure. Consequently, the gas molecules would either be unable to move against the concentration gradient (gas flow on) or be in dynamic equilibrium (gas flow off). Therefore, air bubbles cannot be eliminated by crossing the membrane from blood side to gas side, especially in a short period. This is one explanation of the results obtained in the study. It is indicated that with the introduction of gas boluses, membrane oxygenators may moderate, but they cannot totally eliminate micro bubbles (14).

In this study, there was little difference in numbers or sizes of micro bubbles with respect to temperature of the tested solution (25°, 30° and 37°C) regardless of whether the gas flow was on or off (p>0.05). A possible reason is that this was an in vitro study. The tested blood oxygen saturation was 99-100%, without any oxygen uptake by a patient. Thus, the oxygen driving pressure of the gas side was very low whether the gas flow was on or off. Our results suggest that arterial filters or bubble traps should be used in clinical cardiopulmonary bypass circuits with membrane oxygenators to maximize patient safety.

The results of this study further suggest that the most effective way of deterring introduced air, exiting the oxygenator, from being dispersed into smaller than 40 μm micro bubbles is to increase the blood flow rate to approximately 5 L/min. Many arterial filters impede the passage of larger than 40 μm air bubbles and allow for the venting of trapped air (12,15). However, more study should be done as to the overall results of air entering the arterial filter before there is adoption of this high flow technique in the clinical setting.

REFERENCES


