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CO₂ Clearance by Membrane Lungs

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Abstract

Introduction—Commercial membrane lungs are designed to transfer a specific amount of oxygen per unit of venous blood flow. Membrane lungs are much more efficient at removing CO₂ than adding oxygen but the range of CO₂ transfer is rarely reported.

Methods—Commercial membrane lungs were studied with the goal of evaluating CO₂ removal capacity. CO₂ removal was measured in 4 commercial membrane lungs under standardized conditions.

Conclusion—CO₂ clearance can be greater than 4 times that of oxygen at a given blood flow when the gas to blood flow ratio is elevated to 4:1 or 8:1. The CO₂ clearance was less dependent on surface area and configuration than oxygen transfer. Any ECMO system can be used for selective CO₂ removal.

Keywords

Membrane lung; CO₂ removal; Blood flow; Sweep gas flow; Sweep gas to blood flow ratio

Introduction

The clinical use of prolonged support with membrane lungs (extracorporeal membrane oxygenation, ECMO) began more than four decades ago.^{1,2} ECMO is used to sustain life during severe, acute, cardiac or pulmonary failure leading to recovery or replacement. Membrane lungs replace the physiological function of the lung by fulfilling gas exchange of both oxygen and carbon dioxide (CO₂). When the “sweep gas” flow rate (Q_g) is the same as the blood flow rate (Q_b), the amount of oxygen added and the CO₂ removed are approximately equal. When the ratio of gas flow to blood flow is increased there is no increase in oxygenation, but CO₂ clearance increases in proportion to the gas flow. Selective CO₂ removal with membrane lungs has been used for CO₂ retaining syndromes, and in acute respiratory disease syndrome (ARDS).^{3–6}

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When artificial membrane lungs are used for CO₂ removal, the efficiency is determined by the sweep gas to blood flow ratio ($Q_g: Q_b$), the inlet PCO₂ and the membrane lung properties. The higher the $Q_g: Q_b$ ratio, the more CO₂ is removed. Studies of CO₂ removal performance of commercial membrane lungs are rare. A study was designed to test the CO₂ removal capacity of several commercial membrane lungs over a wide range of $Q_g: Q_b$ ratios.

Methods

Four commercial membrane lungs were tested on a single pass in vitro bench model: Terumo Capiiox RX 05 (Terumo Cardiovascular, Ann Arbor, MI), Maquet Quadrox-iD Pediatric (Maquet, Wayne, NJ), Medos Hilite 2400 (Xenios AG, Stolberg, Germany), Novalung iLA (Xenios AG, Heilbronn, Germany). These devices were chosen to represent a range of devices with a wide range of membrane surface areas. The bench testing system is illustrated in Figure 1. Large volume (20 liter) polystyrene carboys were used along with a centrifugal pump (Terumo Delphin, Terumo Cardiovascular, Ann Arbor, MI), PVC tubing, connectors and heat exchanger (Medtronic BioTherm, Medtronic, Minneapolis, MN) with the selected test device. Fresh heparinized bovine slaughterhouse blood was recirculated through a separate membrane lung to create standardized venous blood conditions (PCO₂ 48 ± 5 mmHg, pH 7.4 ± 0.1 , SaO₂ $65 \pm 5\%$) under other normal parameters (temperature $37 \pm 1^\circ\text{C}$, hemoglobin 12 ± 1 g/dL, base excess 0 ± 3 mmol/L). The test blood was less than 24 hours old and was stored at 4°C prior to use. Following filtration and equilibration, the venous blood was delivered through the test membrane lung at variable $Q_g: Q_b$ ratios (1:1, 2:1, 4:1 and 8:1) at Q_b flows ranging from 0.25–2.0 LPM; this represents typical usage. The ventilating gas was 100% oxygen. Oxygen and CO₂ exchange was measured. Device inlet and outlet pO₂, pCO₂, pH, HCO₃ and oxyhemoglobin saturation were measured on a blood gas analyzer (Radiometer ABL 800 Flex, Brea, CA). The exhaust gas pCO₂ was measured through the same blood gas analyzer and converted to percent CO₂ by dividing the pCO₂ by the atmospheric (barometric) pressure. The actual amount of CO₂ removed per minute was calculated by multiplying the percent CO₂ by the Q_g per minute. Each device was tested in triplicate.

Results

The amount of oxygen transferred per minute for the 4 different devices is shown in Figure 2. Oxygen transfer was unrelated to sweep gas flow and linearly increased with Q_b in all devices. O₂ transfer was unrelated to surface area until the device's "rated flow" for oxygen capacity was reached. No devices reached rated flow at 2 L/min.

The method of determining CO₂ removal is shown in Figure 3 for each device. The exhaust gas PCO₂ and corresponding CO₂ removal over a range of Q_g and Q_b were measured. The CO₂ removed is the percent CO₂ multiplied by the exhaust gas flow. The CO₂ removal at variable blood flow and gas flow for all devices is shown in Figure 4.

The CO₂ removal was essentially the same as oxygen added when the $Q_g:Q_b$ ratio was 1:1. When the $Q_g:Q_b$ ratio was increased to 2:1, 4:1, or 8:1, the amount CO₂ removed increased

proportionately for all devices as shown in Figure 5. No air embolism occurred in these tests, although gas embolism is a possibility if the gas pressure exceeds blood pressure.

Discussion

Membrane lungs are often referred to as “oxygenators” because they are used to add oxygen to blood, although they have another principle function to regulate the CO₂. The amount of oxygen added to the blood is the outlet minus inlet oxygen content difference. Oxygen is carried in the blood in two ways: oxygen bound to hemoglobin and oxygen dissolved in blood. The outlet minus inlet oxygen content multiplied by the blood flow describes the amount of oxygen added per minute. The oxygen content is the hemoglobin multiplied by the oxygen saturation multiplied by a constant (e.g. 1.36 cc/O₂/gram saturated hemoglobin) plus 0.0031 cc/mmHg/dL (the solubility coefficient of oxygen) multiplied by the pO₂.

In a membrane lung, blood enters the device with low oxygen content, then passes through the device and exits with a higher oxygen content. When the device is ventilated with 100% oxygen, the gradient for oxygen transfer is the barometric pressure minus the venous pO₂. The amount of oxygen that can be added is limited by the amount of oxygen that the blood can carry. With fully saturated hemoglobin and a hemoglobin concentration of 15 gm/dL, with a corresponding pO₂ of 600 mmHg, the resulting oxygen content is 22 cc/dL. Under the same conditions, a normal venous blood oxygen content is about 15–16 cc/dL (65–70% saturation with pO₂ 35–45 mmHg). Thus, the maximum amount of oxygen that can be added is about 6 cc/dL. The process of adding oxygen in a membrane lung is limited by the surface area and the maximum delivery capacity, defined as the “rated flow.” The rated flow is defined by the flow of normalized venous blood which exits the device at 95% saturation.⁷

As in the normal lung, the amount of CO₂ removed from the blood is the inlet content minus the outlet content. The CO₂ content in typical venous blood is approximately 57.5 cc/dL.⁸ Carbon dioxide is transported in the blood in three ways: dissolved CO₂, bound to hemoglobin (carbamino hemoglobin), and as bicarbonate. Blood gas analyzers measure the pCO₂ and pH and calculate the bicarbonate using the Henderson-Hasselbalch equation. The CO₂ content can be estimated by converting the mmol (mEq) of bicarbonate to cc of gas using the conversion factor 1mmol = 22.4mL, then calculating the dissolved CO₂ using the solubility factor 0.067 cc/mmHg, and adding about 10–30% (depending on oxygenation status) more to account for carbamino hemoglobin.⁹ Thus, calculating the CO₂ content using blood gas analyzer data can be subject to error.

There is no straightforward method to directly measure the CO₂ content in blood. The original and gold standard method for primary measurement of the amount of CO₂ in blood is to extract all the gases from blood under vacuum, measure the volume, then selectively remove CO₂, calculate CO₂ content by monitoring the change of volume. This is the century old classic method of Van Slyke.¹⁰ Measuring the CO₂ content by this method is rarely, if ever, done today because it is very time consuming, subject to user error, and requires extensive practice to yield precise reproducible measurements. A method of measuring the CO₂ content used in multi-electrolyte analyzers is to measure “total CO₂” by adding an acid to a blood sample which liberates all the CO₂, then expose the CO₂ to a reagent that changes

pH in proportion to the amount of CO₂. The CO₂ measured in this way is reported as mEq of “bicarbonate” (but it is actually not only bicarbonate; it is an indirect measure of CO₂ content). The range of error is about ± 1 mEq/L which is acceptable for clinical interpretation of acid-base balance, but translates to a large error in calculating the actual CO₂ content. For these reasons, calculating the CO₂ removal of a membrane lung using calculated pre- and post-device content differences is subject to large error.

The actual pre-post device CO₂ content difference can be determined by measuring the CO₂ in the exhaust gas and back calculating the inlet/outlet content difference assuming normal venous (inlet) CO₂ content. This was the method used in experiments described in this study

In clinical application, the amount of CO₂ to be removed is matched to combinations of blood and sweep flow. Resting CO₂ production (VCO₂) is approximately 3 cc/kg for adults, 4 cc/kg for children, and 5 cc/kg for infants. Once the amount of CO₂ to be removed is determined, a combination of blood and gas flow may be selected.

Conclusion

When the goal of extracorporeal gas exchange is primarily to remove CO₂ the amount of blood flow required can be much less than that required when the goal is oxygenation. The amount of CO₂ removed at any blood flow is largely dependent on the inlet PCO₂ and sweep gas flow. The CO₂ removal can be as much as four times oxygenation for any of the devices tested. Any pediatric size ECMO system can be used for selective CO₂ removal in children or adults.

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Figure 1.
Test circuit schematic for gas transfer. (See text for explanation.)

Figure 2.

Oxygen transfer in four different commercial devices at Qg:Qb 1:1.

Figure 3.
CO₂ % in exhaust gas at various Qb rates for four devices.

Figure 4.
CO₂ clearance over a range of Q_b and Q_g for four devices.

Figure 5. CO₂ clearance over a range of Q_b and Q_g for all devices. At constant inlet blood PCO₂ (48±5), all devices had the same CO₂ clearance performance.