Institutional report - Assisted circulation

The new advanced membrane gas exchanger

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Abstract

Current membrane oxygenators are constructed for patients with a body surface under 2.2 m². If the body surface exceeds 2.5 m², commercially available devices may not allow adequate oxygenation during cardiopulmonary bypass. To address this, a hollow-fiber oxygenator with an enlarged contact surface of 1.81 m² was tested. In an experimental set-up, six calves of mean weight 85.4±3 kg were connected to cardiopulmonary bypass. They were randomly assigned to a standard oxygenator (n=3; ADMIRAL, Euroset, Medola, Italy) with a surface of 1.35 m² or to an enlarged surface oxygenator (n=3; AMG, Euroset). Blood samples were taken before bypass, after 10 min on bypass, and after 1, 2, 5 and 6 h of perfusion. Analysis of variance was used for repeated measurements. The mean flow rate was 6.5 l/min for 6 h. The total oxygen transfer at 6 h was significantly higher in the high-surface group (P<0.05). Blood trauma, evaluated by plasma hemoglobin and lactate dehydrogenase levels, did not detect any significant hemolysis. Thrombocytes and white blood cell count profiles showed no significant differences between the two groups at 6 h of perfusion (P=0.06 and 0.80, respectively). At the end of testing, no clot deposition was found in the oxygenator, and there was no evidence of peripheral emboli. The results suggest that the new oxygenator allows very good gas transfer and may be used for patients with a large body surface area.

Keywords: Cardiac surgery; Cardiopulmonary bypass, Oxygenator, Oxygen transfer

1. Introduction

According to World Health Organization statistics, obesity has reached epidemic proportions globally, with more than one billion adults overweight and at least 300 million clinically obese. This is a major contributor to the global burden of chronic disease and clearly poses a major risk for serious diet-related chronic diseases, such as type 2 diabetes and cardiovascular disease.

This trend in patient characteristics should encourage cardiovascular surgeons to adapt cardiopulmonary bypass (CPB) in order to provide optimal intraoperative treatment for patients with a large body surface, focusing on adequate tissue oxygenation. The ability to oxygenate a patient adequately on CPB depends on various physiological factors (hemoglobin concentration, the percentage of hemoglobin saturated with oxygen in the arterial blood, cardiac output, etc.) and of the physical characteristics of the oxygenator.

Currently, there are two groups of hollow-fiber membrane oxygenator used in practice. The first type are diffusion, plasma-resistant oxygenators that have been increasingly used for extracorporeal life support or extracorporeal membrane oxygenation for patients who can no longer be supported by mechanical ventilation [1, 2]. The second type are hollow-fiber membranes made of microporous polypropylene that have been widely used for standard CPB; these offer excellent oxygen exchange and carbon dioxide removal even for 6 h [3].

In the present study, a median surface, polypropylene hollow-fiber oxygenator with a biocompatible surface coating (AMG Oxygenator; Euroset, Medolla, Italy) was tested in a chronic CPB scenario in order to prove the usability of this device for patients with a very large body surface area.

2. Methods

The research protocols described were reviewed and approved by the Committee on Animal Care, State Veterinary Office, Lausanne. All animals received care in compliance with the Principles of Laboratory Animal Care formulated by the National Society for Medical Research and the Guide for the Care and Use of Laboratory Animals prepared by the National Academy of Sciences and published by the National Institutes of Health, NIH Publication No. 80–23, revised 1985.

2.1. Animal protocol

This study was conducted on six calves with a mean standard deviation (S.D.) body weight of 85.4±3 kg. All of the
animals were premedicated with xylazine (0.15 mg/kg given intramuscularly). General anesthesia was started with thiopentone sodium (10 mg/kg given intravenously) and maintained thereafter with volatile anesthetic. Isoflurane was mixed with oxygen-enriched air. The animals were fitted with a jugular central venous catheter and a femoral arterial catheter for hemodynamic monitoring, as well as a five-lead ECG. Two investigation groups were established: the control group, using the standard oxygenator \((n=3; \text{ADMIRAL, Euroset})\), and an investigation group \((n=3)\), on which the high-surface oxygenator (AMG) was utilized \([4–6]\).

2.2. Oxygenator

The high-surface oxygenator is an integrated hollow-fiber membrane oxygenator containing a removable hard-shell reservoir and one heat exchanger (HE) integrated into the oxygenating compartment (Figs. 1 and 2). The HE is made of patented stainless steel pipes, with a surface area of 0.08 m².

The performance factor of the HE is 0.64 with a blood flow of 4.0 l/min and a water flow of 10 l/min. The microporous hollow fibers of the oxygenator are made of polypropylene and coated with Agile (phosphorylcholine); they act to separate the gaseous phase from the blood and have a total outer surface of 1.81 m². Their inner and outer diameters are 280 and 380 μm, respectively. This very compact design is intended to ensure an equally high and constant efficiency in heat transmission and gas transfer throughout the entire perfusion process. The static priming volume for the integrated device is 220 ml. This oxygenator can be used with flow rates as low as 3.0 l/min, and its nominal flow rate is 8.0 l/min. The hard-shell reservoir is an integrated venous cardiotomy reservoir (Fig. 2).

In the control group, a low-surface oxygenator used in daily clinical practice (ADMIRAL) was employed. This prototype, used as control device, has the same design except for the following parameters: an oxygenator surface of 1.35 m², with a priming volume of 190 ml and a maximal blood flow of 7 l/min. The contact surface of the HE as well as the performance factor are identical (0.08 m² and 0.64, respectively).

2.3. Cardiopulmonary bypass

Closed chest perfusion was performed in all six animals. For this purpose, the right atrium was cannulated via a jugular vein with a 36-F 340 mm, wire-wound, SmartCanula (SmartCanula, Lausanne, Switzerland), while a 20-F 220 mm arterial SmartCanula was inserted into the carotid artery. Before cannulation, heparin (Liquemin; F. Hoffmann-La Roche & Co., Basle, Switzerland) was given systemically at a dose of 300 IU/kg body weight. Moreover, 100 IU/kg body weight was added to the priming volume. The activated clotting time (Hemochron; International Technidyne Corp, Edison, NJ, USA) was kept above 400 s throughout perfusion.

The CPB circuit was connected after being primed with 1500 ml of crystalloid only (NaCl 104 mEq/l; KCl 5.4 mEq/l; CaCl₂ 1.6 mEq/l; Mg Cl₂ 1 mEq/l; sodium lactate 27 mEq/l;...
The blood flow rate was maintained by a roller pump at 6.8±0.2 l/min. The arterial pH was between 7.35 and 7.45, and the mean femoral arterial pressure was kept between 60 and 80 mmHg. The temperature was maintained at 36 °C. Oxygen flow was supplied to the oxygenator with the gas blender at a flow rate equal to that of the blood flow.

After 6 h of perfusion, the animals were weaned from CPB and decannulated. Heparin was not reversed. The animals were then weaned from the ventilator and extubated. After seven days’ survival, the animals were electively sacrificed for necropsy, with special attention being paid to the kidneys, spleen, lung and heart to detect any focal necrosis suggestive of emboli [7].

2.4. Measurements

Electrocardiogram, central venous pressure, femoral artery pressure, arterial catheter pressure, pump flow, and inlet and outlet pressures of the oxygenator were continuously recorded. A standard battery of blood samples was taken for arterial and venous blood gas analyses, as well as for white blood cell and thrombocyte counts. Samples for hematology were taken before bypass, after 10 min on bypass and after 1, 2, 5 and 6 h of perfusion. Blood gas samples were taken before bypass, hourly during bypass and again 30 min after termination of bypass (spontaneous breathing) and 60 min after bypass (after extubation).

2.5. Data analysis

Mean and S.D. were derived for each parameter analysed. The analysis of variance for repeated measures was used where applicable for determination of statistical significance (P<0.05).

3. Results

The six animals were perfused for 6 h according to the protocol. All animals were weaned from perfusion and extubated. Survival after perfusion was seven days for all calves, at which point they were sacrificed electively for post mortem studies.

The mean flow of the CPB after steady state was 6.8±0.2 l/min. The mean pH varied between 7.35 and 7.45 throughout the run of the perfusion. Mean arterial oxygen saturation could be maintained at >99% in the investigation group, as well in control group. Mean venous oxygen saturation could be maintained above 60% throughout the 6 h in both groups.

The oxygen transfer rate in the investigation group was 55±8.3 cm³/ml/min after 1 h of bypass and 60.9±7 cm³/ml/min after 6 h (Fig. 3). The duration of CPB had no significant influence on the oxygen transfer rate (P=0.5): in the control group, oxygen transfer was 34.8±3.3 cm³/ml/min at 1 h and 33.3±2.4 cm³/ml/min at 6 h of perfusion (P=0.6), and was not significantly different. The oxygenator surface area had a significant influence on oxygen transfer at the end of the perfusion (P=0.006).

The partial pressure of carbon dioxide during the procedure was fell continuously to a minimum value that was measured 6 h after the initiation of the bypass (Fig. 4). There was no significant difference at the end of perfusion (P=0.25) between the two groups (35±1 cm³/ml in the investigation group vs. 40.5±5 cm³/ml in the control group). Post-bypass blood gas analyses showed physiological values and no evidence of major lung trauma or pulmonary edema relative to the 6 h of bypass.

The white blood cell count, after a transient fall, increased to reach a maximal value after 4 h of bypass (Fig. 5). Thrombocyte values exhibited a drop that reached a plateau after 1 h (Fig. 5). Figs. 5 and 6 shows the normalized values of white cell counts and thrombocytes in the two groups investigated. There was no significant difference at the end of perfusion between the groups (P=0.8 for white cell count and P=0.06 for thrombocytes at 6 h of perfusion).

Changes in plasma hemoglobin and lactate dehydrogenase (LDH; Fig. 7) were used as markers for hemolysis. For both parameters, values normalized to the basic results, are presented. After 1 h of bypass in the investigation group, the
hemoglobin level was 65 ± 14 g/l, and at the end of perfusion, we measured a concentration of 65 ± 10 g/l. In the control group after 1 h of perfusion, the corresponding hemoglobin value was 66.3 ± 9 g/l, and at the end of the experiment it was 71.6 ± 8.5 g/l.

Changes in LDH concentration are seen in Fig. 7. After 1 h of perfusion, LDH concentration was 606.7 ± 32 U/l and 653 ± 21 U/l in control group. At the end of experiment, it was 738 ± 10 U/l and 725 ± 27 U/l, respectively (P = 0.8 at 6 h of perfusion). The LDH level in the investigation group decreased in the 1 h of the experiment down to a value of 572 U/l. Following this initial fall, the concentration increased back to the baseline value at 6 h (Fig. 7).

Post mortem studies of four major organs (kidney, spleen, lung and heart) did not demonstrate any macroscopic lesions. No macroscopic defects, such as rupture of the hollow fibers, cracking of the external housing or deposition of clots, were observed after gentle rinsing of the devices with clear water.

4. Discussion

There are three basic considerations in the design of a membrane oxygenator. The first and primary consideration is to provide optimal gas exchange during CPB. Second, the design has to minimize blood trauma during flow and keep the priming volume at the lowest level possible. Finally, the surface of the oxygenator has to be manipulated in order to limit bioactivation due to contact with a foreign surface.

We present here a new oxygenator demonstrating excellent gas exchange ability. The contact surface of 1.81 m² in the device is relatively larger than that of the Euroset commercial product (ADMIRAL) [8] that was used as control device in this study, which had a contact surface area of 1.35 m² and a static priming volume of 190 ml. However, this relatively larger surface area resulted in a much more effective oxygen transfer rate that ranged between 55 ± 8.3 ml/min after 1 h of bypass and 60.9 ± 7 ml/min after 6 h.

Further comparing our results of the oxygen extraction capacity of the lung, which in a normal healthy person

![Graph of blood gas analysis: arterial pCO₂](image)

Fig. 4. The partial pressure of carbon dioxide in the arterial line compared for the two groups investigated during cardiopulmonary bypass.

![Graph of white blood cell count](image)

Fig. 5. White blood cell count values normalized to pre-bypass value, with their evolution in the two groups during cardiopulmonary bypass and on the seventh day after the experiment.
ranges between 110 and 160 ml/min/m², we achieved 37% and 50% of the total capacity of the lung. It should be noted that, according to the literature, the capability of standard available oxygenators for maximum oxygen transfer reaches about 25% of lung capacity.

Moreover, there was no sign of increased blood trauma, hemolysis or thromboembolic events. Damage to thrombocytes occurs in most cases as a result of interaction of the blood with the membrane surface. By using a phosphorylcholine coating, we tried to reduce the inflammatory reaction, which is a normal phenomenon in uncoated systems, and as a result also produced more pronounced platelet destruction.

However, it should be kept in mind that the circulating thrombocyte count is only a partial reflection of alterations in the number of cells adherent to the oxygenator membrane. The extracorporeal circulation usually produces a prompt leukopenia 30 min after the initiation of bypass [9, 10]. This leukopenia is known to be transient and is followed by a leukocytosis caused by the mobilization of a large reserve capacity and the potential for rapid leukopoiesis [11]. This leukocytosis and the drop in the number of the thrombocytes is clearly demonstrated in our experiment and does not seem to be affected by the large contact surface of the polypropylene coating of the membrane.

The results of our study suggest that the large surface area, coated polypropylene oxygenator provides good gas transfer with a low resistance to blood flow using our setup. This larger surface design makes it possible to build a compact large-surface membrane oxygenator with the ability to produce higher blood flows and a low priming volume. Clinical evaluation of this oxygenator will be necessary in the overweight patient population.

References


