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Preliminary Study of a New Extracorporeal Membrane Oxygenator Development When Using Pulsatile Flow

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Abstract

An oxygenator is a very important artificial organ and widely used for patients with lung failure or during open heart surgery. Although an oxygenator has been widely studied worldwide to enhance its efficiency, studies on oxygenators, in particular when using a pulsatile blood flow, are domestically limited. Therefore, a new oxygenator was developed in the lab and animal experimental results are described in the paper. The oxygenator is composed of polycarbonate housing and polypropylene hollow fibers. It has a total length of 400 mm and a surface area of 1.7 m^2. The animal experiment lasted for 4 hours. The blood flow rate was set to 2 L/min and a pulsatile blood pump, T-PLS (Twin-Pulse Life Support), was used. Samples were drawn at the oxygenator's inlet and outlet. The total hemoglobin (Hb), saturation oxygen (sO_2), and partial oxygen pressure (pO_2), partial CO_2 pressure (pCO_2), and plasma bicarbonate ion concentration (HCO_3^-) were measured. The oxygen and carbon dioxide transfer rates were also calculated based on the experimental data in order to estimate the oxygenator's gas transfer efficiency. The oxygen and carbon dioxide transfer rates were 16.4±1.58 and 165.7±10.96 mL/min, respectively. The results showed a higher carbon dioxide transfer rate was achieved with the oxygenator. Also, the mean inlet and outlet blood pressures were 162.79 and 137.92 mmHg, respectively. The oxygenator has a low pressure drop between its inlet and outlet. The aim of own preliminary study was to make a new oxygenator and review its performance when applying a pulsatile blood pump thus, confirming the possibility of a new oxygenator suitable for pulsatile flow.

Key words : oxygenator, pulsatile blood flow, non-pulsatile blood flow, T-PLS, ECLS, CPB

Ⅰ. INTRODUCTION

An oxygenator can perform the function of the human lungs and it is a very important artificial organ in an extracorporeal life support (ECLS) circuit, e.g., cardiopulmonary bypass (CPB), extracorporeal lung assists (ECLA) and extracorporeal membrane oxygenation (ECMO) [1,2]. Oxygen diffuses along a concentration gradient across membranes into the blood flowing through the device and carbon dioxide delivered in the venous blood diffuses along a concentration gradient through the membrane into the gas. In addition, the gas transfer varies in accordance to the total surface area, gas concentration gradients and membrane permeability [3].

The oxygenator was first conceptualized by the English scientist, Robert Hooke and developed as an extracorporeal oxygenator by French and German experimental physiologists in the 19th century. Most of the oxygenators used until the late 1970s were derived from von Schroder's bubble oxygenator and Fry and Gruber's film oxygenator. In the bubble and film oxygenators, 'direct contact' means there is no intervening barrier between the blood and gas compartments and this can cause blood trauma. Therefore, membrane oxygenators adopted a gas-permeable interface between the blood and oxygen. Since the gas does not have any direct contact with the blood in the current membrane oxygenator, blood trauma was decreased and extracorporeal oxygenators have been used for long-term applications, such as in intensive therapy of respiratory distress syndrome. Therefore, the membrane oxygenator has recently

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become the preferred clinical choice [3,4].

Many materials, such as polypropylene, polyolefin, silicone, polymethylpentene, etc., have been used in membrane oxygenators [5-7]. Also, the membrane was coated with heparin to improve the oxygenator's biocompatibility [2,8]. More recently, a study was conducted in regard to the new conceptual oxygenator, the intra-oxygenator. It was conceived to be inserted through the femoral or jugular vein and lodged in the vena cava during gas exchange. In addition, this intra-oxygenator has a smaller blood contact surface than extracorporeal oxygenators. It also reduces the infection risk and surgical operation time, while requiring a nearly zero priming volume. No blood tubes and heat exchangers are required in this system [9,10]. In addition, some researchers introduced a compliance chamber to minimize oxygenator impedance [11], implantable oxygenator [12,13] or a pump-less circuit in the extracorporeal oxygenation systems [5,14].

A new oxygenator was developed in our group and its performance when applying a pulsatile blood pump was inspected in the present study therefore, confirming the possibility of new oxygenator development, which is suitable for pulsatile flow.

II. MATERIALS AND METHODS

A. Oxygenator

The experimental oxygenator was composed of polycarbonate housing and hollow polypropylene fiber membranes. The housing length, internal and external diameters were 260, 45, and 56 mm, respectively. In addition, the inner diameter of hollow fibers was 0.240 mm and the thickness was approximately 35 ㎛. The hollow fiber bundle was assembled with the housing through a potting process by using a polyurethane adhesive agent. The potting was conducted at 1000 rpm for 30 minutes, which was followed by a trimming procedure. Finally, the caps were assembled on the potted oxygenator body, which has a total length of 400 mm and a surface area of 1.7 m^2. Oxygen runs through the inside of the fibers and blood runs around the outside of the hollow fibers in the oxygenator (Figure 1).

Table 1. Average Blood Gas Analysis of the Samples
Hb, hemoglobin sO_2, oxygen saturation; pO_2, partial oxygen pressure pCO_2, partial carbon dioxide pressure HCO_3^-, plasma bicarbonate ion concentration.

	Hb (g/dl)	sO_2 (%)	pO_2 (mmHg)	pCO_2 (mmHg)	HCO_3 (mmol/L)
INLET	10.6 ±0.88	49.17 ±13.30	39.6 ±10.60	44.03 ±7.81	14.73 ±2.72
OUTLET	10.47 ±0.96	105.3 ±1.41	148.63 ±31.33	26.9 ±4.24	11.54 ±2.97

B. Animal Experiment

A canine (weighting approximately 35 kg) was used as a septic shock model by infusing LPS (lipopolysaccharide) which was diluted in 100 ml of normal saline. The femoral vein and the femoral artery were dissected for cannulation and 15 and 17 Fr catheters were inserted. Before the animal experiment, normal saline with heparin (50,000 IU/L) was circulated through the entire system for anticoagulation. The animal was heparinized, with 250 units/kg for the initial anticoagulation, and infused with heparin at 30 ml/h during the experiment. Ketamin 5 cc and Xylazine 1.8 cc were used as anesthesia and it was maintained by inhalation of N_2O gas and Enflurane. The animal experiment lasted for 4 hours and blood was circulated at a flow rate of 2 L/min. During the animal experiments, pressures were monitored at the oxygenator inlet and outlet. Ten milliliters of blood was drawn

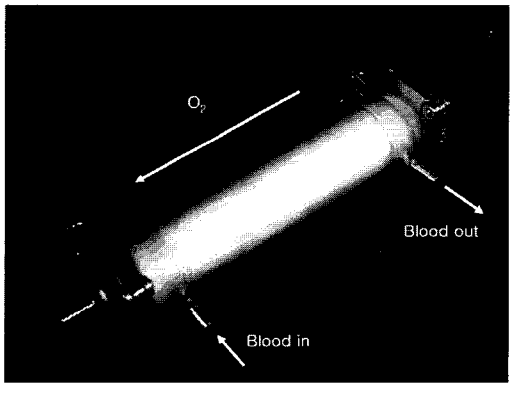

Fig. 1. Side View of the Experimental Oxygenator: Arrows indicate the direction of oxygen and blood flow through the device, respectively. Oxygen runs through the inside of the fibers and blood runs around the outside of the hollow fibers in the oxygenator.

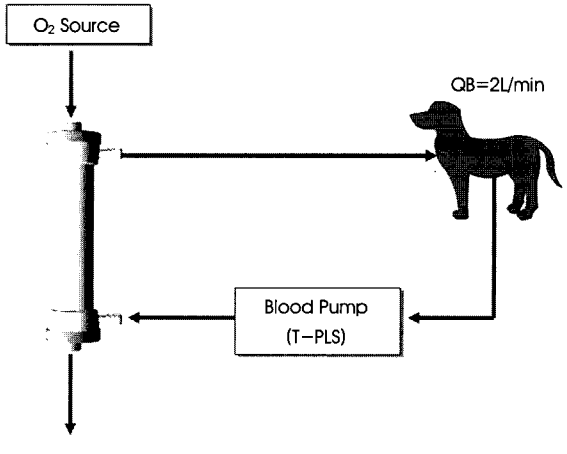

Fig. 2. Schematic Illustration of the In Vivo Experiment Circuit : QB, blood flow rate; Blood pump, T-PLS (pulsatile blood pump).

upstream and downstream of the oxygenator. Samples were analyzed by using automatic blood gas analysis (ABL520, Radiometer Limited, UK) for total hemoglobin (Hb), saturation oxygen (sO_2), partial oxygen pressure (pO_2), partial carbon dioxide pressure (pCO_2), and plasma bicarbonate ion concentration (HCO_3^-). Moreover, oxygen transfer rates and carbon dioxide transfer rates were calculated. The scheme for the animal experiment is shown in Figure 2.

C. Blood Pump

The T-PLS (Twin-pulse life support, Newheartbio, Korea)was used as a blood pump in the present study (Figure 3). It consists of an electrical power supply, a control panel, an actuator and two blood sacs. The reciprocating actuator alternatively squeezes on the left and right blood sacs. When the actuator squeezes the left sac, the blood in the sac can move only in a forward direction because of polymer check-valves, which prevent blood from flowing backward; at the same time, the right sac expands and blood fills it. In the same manner, blood in the right sac moves forward when the actuator squeezes that sac and in this alternate fashion the actuator creates a pulsatile flow. The advantages include an easily adjustable pump rate, an auto-priming mode, a suction detection mode, an alarm and flow estimation. This device is used in a lot of research and in many experiments for pulse flow [15]. Furthermore, it received manufacturing approval from the Korea Food and Drug Administration in 2004 and has been used in clinics.

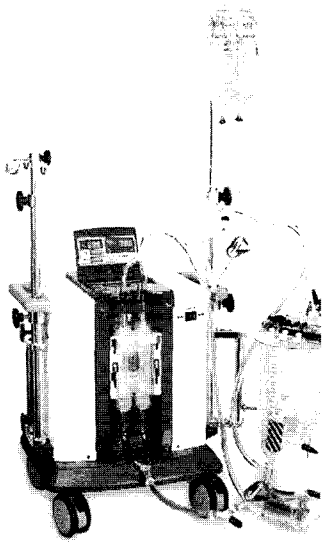

Fig. 3. Pulsatile Blood Pump, T-PLS (NewHeartBio, Korea) : The pulsatile blood pump is composed of blood sacs, an electrical power supply, a control panel, actuator, and polymer check-valve in each sac.

D. Equations

The gas transfer rate was calculated as follow:

- Oxygen content (Vol %)
  $= (Hb \times 1.34 \times \%O_2 saturation)/ 100 + pO_2 \times 0.003$
- Oxygen transfer rate (ml/min)
  $= QB \times (Arterial\ O_2\ content - Venous\ O_2\ content)$
- Total carbon dioxide (mmol/L)
  $= HCO_3^- + 0.03 \times pCO_2$
- Carbon dioxide transfer rate (ml/min)
  $= 22.4 \times (Venous\ tCO_2 - Arterial\ tCO_2) \times QB$

Hb: hemoglobin (g/dl), pO_2: partial O_2 pressure (mmHg), pCO_2: partial carbon dioxide pressure (mmHg), QB: blood flow rate (L/min), HCO_3^-: plasma bicarbonate ion concentration (mmol/L)

All data are presented as mean ± standard deviation.

III. RESULTS

During the experiments, there were no technical problems concerning the new oxygenator. In addition, no plasma leakage or membrane rupture was observed and the animal was well sustained in all circulation sessions. The results for blood gas analysis are provided in Table 1. Hemoglobin (Hb) levels were found not to be significantly different between the oxygenator inlet and outlet. After the blood was run through the oxygenator, the mean oxygen saturation level was sufficiently maintained. The inlet pO_2 indicated the blood was deoxygenated but the increase in pO_2 through the oxygenator indicates the blood was adequately oxygenated. A similar trend was observed for the pCO_2 levels upstream and downstream of the oxygenator. The inlet and outlet oxygen contents were 7.01±1.83 and 15.21±1.28% respectively. Likewise, the inlet and outlet total carbondioxide were 16.04±2.46 and 12.36±2.92 mmol/L, respectively. The results of the HCO_3^- used were used to calculate the total carbon dioxide. The average O_2 and CO_2 transfer rates were shown in Table 2. Also, the oxygenator has a low pressure drop between the oxygenator inlet and outlet. The mean inlet and outlet blood pressures were 162.79 and 137.92 mmHg, respectively and thus the pressure drop across the oxygenator was approximately 24.87 mmHg. The representative inlet and outlet pressure profiles are show in Figure 4.

Table 2. Average O_2 and CO_2 Transfer Rate of the Device

	O_2	CO_2
Gas transfer rate (mL/min)	16.4±1.58	165.7±10.96

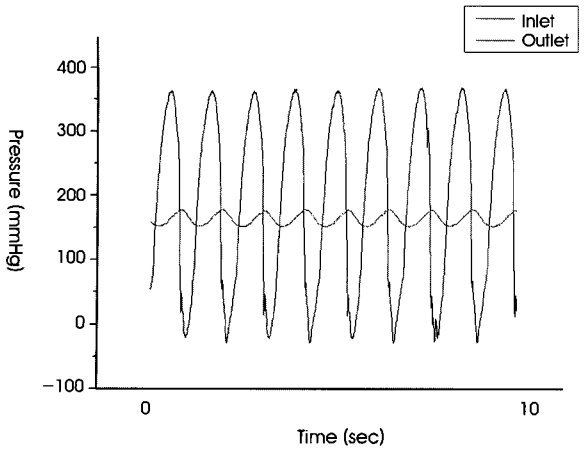

Fig. 4. Representative Device Inlet and Outlet Pressure versus Time : The mean inlet and outlet pressures are 162.79 and 137.92 mmHg respective.

Ⅳ. DISCUSSION

During the last decades, previous studies on pulsatile perfusion revealed the advantageous effects of blood pulsation during ECLS circuits [16]. When the pulsatile flow was used in CPB, microcirculation into end organs was improved. Besides, metabolism in vital organs, such as, the brain, heart, liver, kidney and pancreas, was also enhanced. The pulsatile flow was reported to have a positive influence on reducing edema formation, systemic inflammatory response syndrome and postoperative death, as compared with CPB with non-pulsatile blood flow [17-20]. Pulsatile perfusion is also suggested in an ECMO or a VAD support, because it can produce more physiologic hemodynamics [21]. Recently, the pulsatile perfusion was successfully applied in clinic practice [22].

Although the advantageous effects of pulsatile flow on blood perfusion have been widely discussed, most of the conventional ECLS circuits are adopting roller and centrifugal blood pumps. This may be caused by larger blood damage with a pulsatile blood pump [19]. A previous study also compared the oxygen transfer rate under the steady flow with that of pulsatile blood flow, when using a commercial oxygenator which contained an air chamber to reduced blood cell trauma. Their results revealed the average oxygen transfer rate was reduced by 10% with pulsatile blood flow [23]. In addition, the structural designs of current hollow fiber membrane oxygenators may also have a direct impact on the pulsatility. Therefore, when the pulsatile flow is applied in the ECLS circuit, the oxygenator which is optimized more for pulsatile blood flow is required for less blood trauma and high gas transfer efficiency. Thus, the present study was performed by using the pulsatile blood flow to verify the oxygenator efficiency.

The O_2 transfer rate with the oxygenator in the present study was relatively low, when compared with other commercial oxygenators [14]. This might be caused by the low blood flow rates and high venous blood O_2 content. However, the CO_2 transfer rates are promisingly high and thus the oxygenator may be useful for arteriovenous CO_2 removal (AVCO2R) treatment for patients with end stage chronic obstructive pulmonary disease (COPD). In addition, the blood pressure drop across the oxygenator was less than 24.87 mmHg, which is lower than that in other commercial oxygenators [6,24]. Unlike a commercially available oxygenator, which has a complex blood flow pathway, the experimental oxygenator is characterized by a simple blood path because the blood pathway in the oxygenator is straight. A low pressure drop between the oxygenator inlet and outlet is assumed to result from this simple blood pathway. In addition, a simple blood pathway is believed to enhance hemolytic characteristics with the oxygenator. The oxygenator presented in this study is still an experimental prototype and further optimizations are required in order to increase the oxygen transfer rate and to improve biocompatibility. However, the new oxygenator is assumed to be not only less blood traumatic but also more suitable for pulsatile flow.

This animal study was conducted with a focus on the gas transfer ability of the experimental oxygenator. The results obtained in the present study revealed adequate gas transfer efficiency with the oxygenator, in particular, a high CO_2 transfer rate. Moreover, the experimental oxygenator is a useful trial to develop a new oxygenator which has the improved gas transfer efficiency of gas transfer and reduction in blood hemolysis, when using a pulsatile blood pump.

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