생체 실험을 통한 좌심실보조기의 평가

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Evaluation of Left Ventricular Assist Device through *In Vivo* Experiments

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Abstract

In this article, we present and analyze the results of the three consecutive *in vivo* experiments of the LVAD to evaluate the function of the LVAD and the adverse effects on living animals. We applied the LVAD consecutively to three mongrel dogs and the circulation of the blood was assisted under the anesthesia. We used in general both the asynchronous mode and the synchronous mode to drive the LVAD. During the experiments we monitored the dogs with a polygraph to evaluate the function of the LVAD and the additional effects on the natural hearts. We also examined several clinical pathologic tests in order to see the effects of the LVAD to the red blood cells and the other internal organs.

The dogs survived for two to three days. The LVAD assisted the circulatory system at the maximum assist flow rate of 3.0 l/min. Although the red blood cells of the dogs had mechanical damages by the LVAD to result in the hemolysis, the degree of the hemolysis was not so high and the damages caused by the hemolysis on the dogs were not serious. The myocardium of the first dog was gradually worsened and eventually failed. The damage of the myocardium was due to the asynchronous driving mode of the LVAD. The other organs did not have serious damages due to the application of the LVAD.

The main purpose of this paper is to evaluate the results of the *in vivo* experiments of the LVAD and to find better ways to the application of the LVAD to human beings.

Introduction

It has been known that about 1.0 % of patients who undergo the open heart surgery become unweanable from the cardiac bypass system due to the heart failure during the surgical procedure. And nearly 20 % of the patients who are supposed to have cardiac transplantations die while waiting for a donor of the natural heart. In these cases the left ventricular assist devices (LVAD) may be essential for the extension of the lives of these patients.

The LVAD is the device which compensates a portion of the malfunction of the left ventricle through pumping a part of the blood of the natural heart between the aorta and the left atrium or the left ventricle. The LVAD is classified into two types according to the driving system. The first type is an air-driven or pneumatic ventricular assist device which uses an air pump to supply the blood. The second type is an electrohydraulic ventricular assist device which uses an electrohydraulic pump. The pneumatic VAD has a simple structure and is driven easily without the problem of the suction. However it needs a large external air driving pump. So the patient with the pneumatic VAD cannot move freely and the system is hard to control exactly. The electrohydraulic VAD adopted the power of an electrohydraulic pump. Since the fluid of the electrohydraulic pump is not compressible the control of the VAD is exact. The electrohydraulic pump is smaller than the pneumatic pump. So the application of the electrohydraulic pump is easier than that of the pneumatic pump. But the VAD having an electrohydraulic pump has a complicated structure and is more expensive than that of the pneumatic pump.

In our experiments we used the electrohydraulic VAD which is developed in the department of the biomedical engineering, Seoul National University. We applied the LVAD to three mongrel dogs and evaluated the effect of the LVAD on the living animal.

Materials and Method

The Assist Device is powered by the hydraulic energy which means the movement of fluid in the blood pump contracts and distends the blood sac in an acryl chamber. The prototype of the electrohydraulic VAD is composed of the following three elements:

1) blood pump 2) pressure pump 3) control and monitoring unit (CMU)

1) Blood Pump

Blood pump drains blood from the left atrium or the left ventricle and provides the aorta with the blood. The amount of the circulatory assist should be enough for supporting patient's circulation. For the animal experiments using the mongrel dogs the blood sac of 50 ml is made of the segmental polyurethane (Pellethane®, Dow chemical, USA). The outer housing containing the blood sac is made of the transparent acryl of 90 mm x 65 mm x 115 mm through which the pattern of the compression or distention and the filling status of the blood sac can be checked easily by the pump perfusionist so as to adjust the control parameters. Polymer valves are used at the inflow and the outflow port.

2) Pressure Pump

In the pressure pump the high positive pressure and the negative pressure are generated by the movement of the polyurethane bellows and the generated pressure is transferred to the blood pump by the transmitter, i.e., water. The pressure pump which works as an electrohydraulic energy converter consists of a DC motor, a ball screw and a polyurethane bellows. The polyurethane bellows, 100 ml of volume, is manufactured using a duralumin mold and is filled with water. The ball screw converts the rotary motion of the motor to the linear movement of the bellows. When the motor rotates in one direction the pusher plate joined to the ball screw compresses the polyurethane bellows. The reverse rotating of the motor makes it possible for the polyurethane bellows to be distended. The tygon tube, 10 mm of the diameter and 1 m of the length interconnects the blood pump and the pressure pump. The DC motor of pressure pump rotates several revolutions for the pump ejection. An encoder (Gold Star S-30-200 KO, Korea) attached to the outer side of the motor axis gives the information about the motor speed and the direction of the motor rotation to the control and monitoring unit (CMU).

3) Control and Monitoring Unit

The CMU controls the pump output and the pumping patterns by changing parameters such as systolic velocity, diastolic velocity and stroke length. The CMU as a main control center shows the systolic velocity and the diastolic velocity and the limb lead electrocardiograph to the pump perfusionist and gets control orders from the pump perfusionist and sends control parameters to the microprocessor controller. Basically a notebook PC (IBM 386) as a communication port to the operator, a motor driving unit and a microprocessor controller composes the CMU. The operator also can change the synchronization rate from 1:1 to 3:1 and change the mode of asynchronization and adjust the pump beating delay time for an effective synchronization. The motor is supplied by 24 volt DC power source and all the system is supported by the uninterruptible power supply.

4) Animal Experiments

Three mongrel dogs (weight: 25 - 35 Kg) were anesthetized with the sodium pentothal 250 mg and maintained with the halothane via the endotracheal intubation. A catheter was inserted into the femoral artery to measure the arterial pressure. A Swan-Gantz catheter was inserted via the jugular vein to measure the LAP and cardiac output using the thermodilution method. The electrocardiograph (ECG) was continuously monitored. The skin incision was done through the fifth intercostal space to show wide view of the chest cage. A 32-Fr. cannula was inserted into the left atrium for the drainage of the blood to the LVAD. The blood pump of the LVAD was put on the operating table beside the animal. The other part of the LVAD, i.e., the pressure pump and the CMU, were rested on a small portable table. The descending thoracic aorta was cannulated with a half inch diameter cannula of which anastomotic end is attached a porous polyurethane tube. During the operation the Hartmann solution was administered to get an appropriate blood pressure. After the cannulation of the aorta the inflow cannulation at the left atrium was performed. Finishing the cannulation of the inflow and outflow, the cannulae were connected to the blood pump of the LVAD. After the air removal the LVAD started. The current, the position of the pusher plate, and the speed of the motor were monitored and adjusted continuously by the LVAD operator. The status of the animal during the assistance of the circulation with the LVAD was checked with the clinical pathologic examination. The items of this examination are as follows; the arterial blood gas

analysis, the complete blood count, the blood clotting test, and the chemistry of the serum. After the surgical procedure the animal was maintained under the anesthesia for avoidance of adverse effects caused by the movement of the animal.

Results

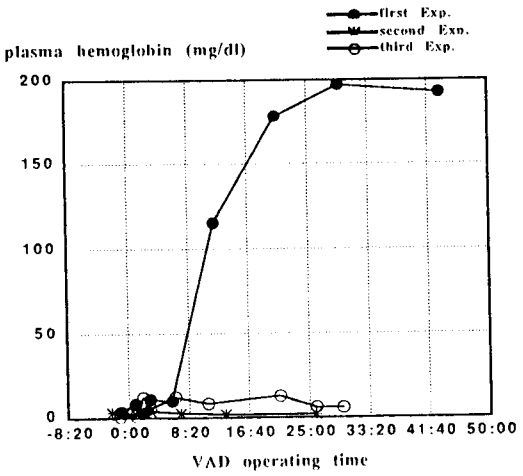
The first dog survived for three days. After the surgical procedure had finished, the assist of the LVAD was performed at the flow rate of 2 - 3 l/min with the asynchronous mode. About forty hours of the LVAD application the blood pressure decreased to 40 to 80 mmHg. At the same time the arterial blood gas analysis shows the acidosis with the pH range 7.06 - 7.18. The electrocardiograph shows the arrhythmia. The dopamine administration was started for increasing the contractility of the heart. Five hours later, however, the dog died.

The level of the plasma hemoglobin gradually increased during the experiment upto 200 mg/dl. The levels of the creatinine kinase (CK) and the lactate dehydrogenase (LDH) were continuously rising very high. The other laboratory examinations showed no evidence of other internal organ damages. We verified with an autopsy that the myocardium was damaged and that there was no other internal organ damages.

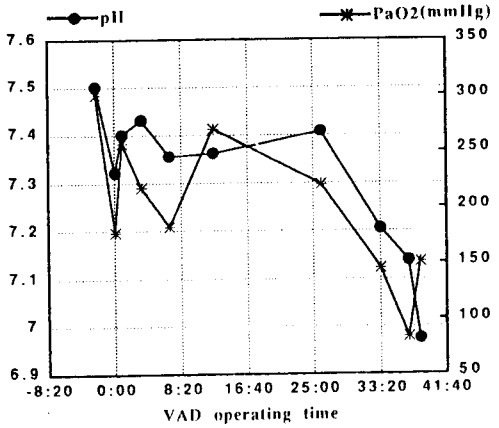
The second dog lived for two days. The assist of the LVAD was the same as the first dog. After thirty three hours of the LVAD application the acidosis was detected. The pH range was below 7.2. We administered the bicarbonate solution to adjust the acid-base balance. Six hours later the dog died of the severe acidosis.

The laboratory examinations revealed no evidence of an abnormality except for the arterial blood gas analysis. After the detection of the acidosis, the pH fell to 6.98 and the partial pressure of the oxygen in the arterial blood dropped to 80 mmHg approximately. The plasma hemoglobin level was lower than 10 mg/dl. The levels of the CK and the LDH rose but the amount of the increase was less than that of the first case. We could not find the damages of other internal organs on the gross examination at an autopsy.

The third dog lived for two days. The LVAD assisted the circulation of the blood at the flow rate of 1.5 - 2 l/min with the synchronous mode. In this case the laboratory examination showed that the status of the dog was better than that of the former two cases. However, a little but continuous bleeding was detected with an inserted chest tube. Twelve hours later the total amount of the bleeding was 1.5 l. We gave a transfusion of two pints of blood to the dog. The bleeding continued through the site of the cannulation. So we did the surgical operation again for the removal of the cannulation, i.e., the removal of the LVAD. After thirty hours of the application the LVAD was removed and the dog was awakened. The dog died of the pulmonary congestion next day.



<Fig.1> the data showing the hemolysis of three experiments



<Fig.2> the data showing the respiratory failure of the second dog

The level of the plasma hemoglobin was less than 15 mg/dl. The levels of the CK and the LDH were rising and were lower than that of the first case. The other laboratory examination revealed no evidence of an abnormality except for the hemoglobin level. The hemoglobin level was 13 g/dl initially and dropped to the lower level than 7 g/dl after the 8 hours of the application of the LVAD. We found the congested lung on the gross examination at an autopsy and there was no evidence of the damage of other internal organs.

Discussion

We have three cases of the application of the LVAD. In the first case the dog died of the left ventricular failure. This left ventricular failure was brought about by the operation of the LVAD on the asynchronous mode. On the asynchronous mode the LVAD is not synchronized with the natural heart. When the filling period of the blood sac of the LVAD coincided with the systole of the natural heart the LVAD deprive the natural heart of some blood. As a result the coronary circulation was impaired and the heart was damaged.

In the second case we found, after the death of the dog, that the bellows of the ventilator was perforated. So we considered the respiratory failure as the main cause of the death of the second dog. The data of the arterial blood gas analysis, i.e., pH and PaO_2, support our consideration.

In the third case the main problem was the bleeding at the site of the cannulation. The bleeding was hard to stop. We had to remove the cannulae without an additional application of the LVAD. In this case the operation of the LVAD was done in the synchronous mode. Since the coronary circulation would not be impaired in the asynchronous mode we concluded that there would be no left ventricular failure in the third dog.

The problem of the hemolysis was detected only in the first case and this was not a severe condition. We could tolerate the hemolysis of this extent. In the second and the third case one can see the negligible amount of the hemolysis and this was considered to be brought about by the polymer valve.

In conclusion the synchronous mode is better than the asynchronous mode for the natural hearts. We should operate the LVAD in the synchronous mode. And we also suggest that the LVAD be operated in the preload sensitive condition to avoid the suction of the left atrium. We are preparing other animal experiments to evaluate this idea.