ABSTRACT

A permanently implantable intrathoracic left ventricular assist device (LVAD) for human use has been developed and evaluated in vitro and in vivo. A seamless layer of glutaraldehyde-treated gelatin as the blood contacting surface and the use of valves made of human dura mater eliminates the need for anticoagulation. The pump was designed to fit the chest wall interposed between the cardiac apex and the thoracic aorta. In vitro performance and flow visualization studies have shown satisfactory pump performance. Left ventricular unloading was well demonstrated in in vivo experiments. Laboratory data for chronic experiments were within normal limits. Four long-term animals are continuing for periods of 1-3 months.

Key words: intrathoracic LVAD, pusher-plate, permanent human use, biolization, energy conversion.

INTRODUCTION

Since the first left ventricular assist device (LVAD) was implanted in a patient in 1963 by DeBakey, extensive research has been done in the design and development of assist devices for human use. Some patients recover from severe circulatory failure using a LVAD and can be successfully weaned from the device. However, the number of long-term survival cases after assist pump removal is limited. The unfavorable results may be due to many factors such as preexisting extensive left ventricular damage, hemorrhagic tendencies after prolonged cardiopulmonary bypass, concomitant right ventricular failure and multi-organ failure from insufficient circulatory support in terms of effectiveness and duration. Therefore a need exists for both an intermediary and a long-term LVAD. The devices may aid patients awaiting cardiac transplantation or suffering with rejection crisis.

Our current efforts are directed to the development and evaluation of a LVAD for intermediary and permanent human use,

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emphasizing hemodynamic effectiveness, durability and blood compatibility of the device. Our previous "biolized" hemispherical LVAD4 continuously operated for over 10 months in a calf without anticoagulation. The purpose of this paper is to describe a new biolized intrathoracic pusher-plate LVAD for permanent human use and to report the in vivo results using calves.

MATERIALS AND METHODS

The current intrathoracic pusher-plate LVAD consists of an outer and inner housing, pusher-plate, diaphragm, and actuator (Fig. 1, 2). The pump fits the curvature of the human chest wall with the actuator located para-thoracically. The housings are made of epoxy (HysolR). The inner housing is covered by a textured layer of Avcomat 610R. The pump diaphragm is made of a texturized polyolefin rubber. The blood contacting surface is covered by a seamless layer of glutaraldehyde-treated gelatin impregnated into these textured base materials. The actuator is a pneumatic cylinder with a stroke of 0.6 inches and provides a positive displacement of the pusher plate only in the systolic direction. During diastole, the actuator shaft is disconnected from the pusher-plate shaft to allow the actuator piston to be quickly retracted by vacuum, allowing the pusher-plate to return passively by the inflow pressure. In order to monitor the position of the
pusher-plate, a Hall effect sensor (American Aerospace Controls) is bonded to the outer housing. A high energy samarium cobalt magnet incorporated on the back of the pusher-plate provides the magnetic field for the sensor. For inflow and outflow valves, 22 mm ID trileaflet valves made of human dura mater are used. The inflow valve is located inside the inlet port of the inner housing. Both inlet and outlet ports of the inner housing were designed based on anatomical and fluid dynamic considerations. The anatomical location of the apex, the descending aorta, and the axis of the left ventricle were obtained from studies of human CT scans.

IN VITRO EVALUATION AND RESULTS

In vitro performance testing of the pump was conducted in a mock circulatory rig maintaining inlet and outlet pressure at 15 mmHg and 120 mmHg, respectively. At 230 msec of fill time, full stroke was achieved resulting in a net output of 80 ml per stroke of the pump. At 120 BPM, the pump output was 9.6 L/min satisfying the required pump function. A clear plastic pump housing was assembled with the pneumatic actuator for flow visualization studies using Amberlite particles (100-500 μ) in a 60% water, 40% glycerin solution. A generally good washout of the inside was obtained.

IN VIVO EVALUATION AND RESULTS

With pumps designed to fit the human anatomy, a modification of the inflow tract for in vivo calf experiments was necessary. For short term experiments, an 8 cm extension tube was required to connect the apex to the inlet port of the pump. The inflow tract had an ID of 22 mm throughout in order to eliminate step formations which would promote early stenosis due to thick depositions. The outflow tract consisted of an outflow valve, a valve housing and an outflow graft. The graft was a 26 mm ID low porosity woven Dacron arterial graft 18cm long. For the long term in vivo experiments, a completely different inflow system was used consisting of an epoxy cannula with beveled tip, Biomar coated impervious woven Dacron graft supported by a stainless steel wire, and an epoxy inflow elbow. The internal surface of the epoxy tubes was covered by a texturized surface of Avcomat 610 and impregnated with glutaraldehyde-treated gelatin. These components are all 22 mm ID and connected by threaded quick connectors.

Pump Implantation Procedure: Under general anesthesia, a left lateral thoracotomy was made through the sixth intercostal space. The animal was fully anticoagulated with heparin (3mg/kg). The outflow graft was sutured to the descending aorta end-to-side.
at the level of the sixth rib. In the short-term series, an apex ring was sutured to the apex of the heart. Then, the myocardium was cored and the inflow cannula was inserted to the left ventricle using an insertion tool. In the long term experiments, a purse-string suture was placed around the apex and the heart was clamped softly near the apex. An incision was made on the apex and the cannula was introduced into the left ventricle as soon as the clamp was removed. The inflow connection was made using a balloon system and cardiopulmonary bypass was not used. After partial resection of the sixth and seventh rib, the pump was fixed to the chest wall with the actuator placed parathoracically. Protamine sulfate was usually given to neutralize the heparin. Anticoagulants were not used postoperatively. Hemodilution and autotransfusion during surgery eliminated homologous blood transfusions except in two cases (Exps. 78317 and 79367). Instrumentation included a pressure transducer (P-6.5 Konigsberg Instruments) in the left ventricle and an electromagnetic flow probe (model NQ, In Vivo Metric Systems) on the outflow graft and a myocardial EKG lead ("O" Flexon American Cyanamid) for monitoring EKG and synchronization.

ANIMAL STUDIES

In six short-term experiments, synchronized counterpulsatory left ventricular bypass was continued for 22 to 50 days to evaluate and finalize the new pump design (Table 1). All animals were sacrificed electively. Three calves were terminated earlier than 6 weeks due to complications. One animal was sacrificed due to rupture of the outer housing. Based on this experience, the wall thickness of the outer housing was increased and the actuator mounting boss was redesigned. A second case was terminated at 33 days because of low flow which began after 3 weeks. At autopsy localized thick depositions were found at the proximal inflow graft surrounded by fungal abscesses. Sacrifice of a third animal at 22 days was because of sustained high fever. At autopsy, a diffuse subendocardial and myocardial hemorrhage was found on both right and left ventricles. The pathological diagnosis was bacterial endocarditis due to gram negative bacilli.

During initial 4 short-term experiments, we realized that some deposition developed at the diaphragm-housing (DH) junction. A redesigning of the inner housing was performed to eliminate a narrow gap of the D-H junction. The pumps with revised housings were implanted in two subsequent short-term experiments and this modification proved very effective (Fig. 3). Another problem was the thick deposition inside the inflow graft. The first animal with the new inflow tract was sacrificed at 35 days of bypass. The inflow restriction was caused by valve stenosis due to bacterial infection. The new inflow cannula and elbow were clean despite the infection and valve stenosis. Presently four long-term experiments are continuing for over 1-3 months without any sign of inflow stenosis or pump deterioration. The impervious noncollapsible inflow tract appears very successful in preventing the thick depositions.

### Table 2

<table>
<thead>
<tr>
<th>Experimental No.</th>
<th>BW (kg)</th>
<th>Bypass flow (ml/min)</th>
<th>LV unloading (TI)</th>
<th>LV unloading (IV)</th>
<th>Diastolic augmentation (%)</th>
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* daily average, † maximal percent reduction in TI and IV on by synchronized left ventricular bypass, ‡ maximal percent increase in aortic diastolic pressure by countershock... no LV measurement.
Hematological and biochemical studies: The hematocrit (Hct) dropped immediately after surgery and recovered slowly at 3 weeks. After 4 weeks the Hct was not significantly different from that of the preoperative values. The hemoglobin concentration and erythrocytes showed similar tendencies. Leucocytes increased on the first postoperative day but returned to normal within a week. Serum free hemoglobin did not increase throughout the experimental period. Platelets fell immediately after implantation, then recovered to normal within a week. No significant drop in fibrinogen value was noted. Total protein was low during the first week, and recovered by the second week. Albumin had a similar tendency. Bilirubin was elevated immediately after surgery, but returned to normal within 2 weeks. There was no abnormal elevation of BUN, creatinine, or uric acid. Electrolytes remained normal (Fig. 4).

Hemodynamic Studies: During the first week, tachyarrhythmias were occasionally observed. Whenever the heart rate exceeded 140 BPM, the pumping was changed to the asynchronous mode. The pump flow was 5.5 L/min at implant, then increased to 9.2 L/min by the second week. Displacement of the pusher-plate reached a maximum within a week while heart rate gradually decreased thereafter. The maximum TTI and LVEDP reduction from the pump off to pump on was 71% and 52%, respectively. Aortic diastolic pressure increased 44% by counterpulsation (Table 2).

COMMENTS

Under the concept of "biolization", we have developed a glutaraldehyde-treated gelatin layer for the blood contacting surface of the pump and thus successfully extended in vivo testing of the hemispherical LVAD to over 10 months without the use of anticoagulants. The problem we encountered at the end of such long-term experiments was calcification in the depositions which possibly occurred secondarily to the disruption of the gelatin layer by chronic mechanical stress accumulating in high flexing areas of the diaphragm. Problems associated with material endurance have been observed in different types of blood pumps by other investigators and remains a serious problem for its long term use. The diaphragm of the new pump has a maximum extension ratio of 15% which is acceptable since the gelatin layer has a maximum extension ratio of more than 60%. Using current coating methods, we can avoid cracks in the gelatin which may cause deposition and calcification, the major factors contributing to mechanical failure of the blood pump in long-term implants.

An LVAD should maintain peripheral circulation and promote the natural healing process of the ailing heart. Theoretically this will be accomplished by resting the left ventricle while supplying enough blood flow to the heart and other organs. The extent of left ventricular unloading and augmentation of coronary perfusion depends upon the relative difference in impedance between the natural outflow and the inflow of the LVAD. This is affected by synchronization, the positioning of the inflow cannula, valve performance, the resistance of the pump diaphragm and the stroke volume of the left ventricle. The reduction in TTI from the pump off to the pump on can indicate the degree of left ventricular unloading. In this series of experiments, the reduction in TTI and LVEDP and augmentation of diastolic aortic pressure were well achieved. The pump flow satisfied the physiological needs for typical adults.

At the present time, various electromechanical and thermal energy converter systems are under development. By mounting the actuator parathoracically as in our design, the pump could easily be mated to practically all the existing or being developed drive systems, and moreover, the actuator can be replaced without entering the chest.

REFERENCES


ACKNOWLEDGEMENT

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