33rd Annual International Conference of the IEEE EMBS
Boston, Massachusetts USA, August 30 - September 3, 2011

In vivo Performance Evaluation of the Innovamedica Pneumatic Ventricular Assist Device

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Abstract— **We evaluated the *in vivo* performance of the Innovamedica pneumatic ventricular assist device (VAD), a new prototype of a simple, low-cost device for hospital circulatory support programs. We implanted the Innovamedica VAD in 6 sheep (weighing 55 to 91 kg). The inflow cannula was placed in the left ventricle, and the outflow cannula was anastomosed to the descending thoracic aorta. After heparinization (3mg/kg), we initiated the pump and monitored its hemodynamic performance for 6 hours. In a subsequent study we implanted the device for left ventricular support in two sheep for a 30-day period. We evaluated device performance based on implantation procedure, hemodynamic performance, and hematological impact. We monitored hematological and biochemical variables, and we assessed hemolysis. In the short-term experiments, the pumps maintained a mean blood flow of 4.4 ± 0.8 L/min. During support, mean arterial blood pressure was 76 ± 15 mmHg. The overall average concentration of plasma free hemoglobin was 5.11 ± 0.6 mg/dl compared with a baseline value of 4.52 ± 0.7 mg/dl. In the 30 day trials, mean blood output was 4 l/min ± 0.2, plasma free hemoglobin was 5.9 ± 4 mg/dl for the 30 day period excluding the first 48 hours. Warfarin/Aspirin anticoagulation was used after the first 72 hours with an average INR of 2.9 for the entire test period. Post-mortem showed no blood clots or any significant tissue damage to brain, lungs or kidneys. The devices operated without any significant adverse events in all of the experiments. The Innovamedica VAD was easy to implant and de-air and was found to be effective, reliable and biocompatible.**

I. INTRODUCTION

Mechanical circulatory support is an important alternative treatment for heart failure in patients who do not improve with pharmacologic therapy and who may not survive the long wait for a heart donor (1). By replacing or supporting heart function, assist devices provide adequate perfusion to organs and maintain the patient in stable condition. In some patients, mechanical support promotes recuperation of the cardiac muscle (2-4). Mechanical assistance can be maintained for days to weeks or longer (weeks to months) (5). The Innovamedica pneumatic ventricular assist device is a new prototype of a simple, low-cost, device for hospital circulatory support programs. This paracorporeal cardiac assist device is intended to be used for short-term operative support (a few hours), acute and post-cardiotomy support (up to about 2 weeks), and long-term support (3 months to several years). In addition, it can be used as a left ventricular assist device (LVAD), a right ventricular assist device, or a biventricular assist device (6).

The Innovamedica pneumatic ventricular assist device (VAD) is a new low cost device that has been designed as an option for all mechanical support applications, and includes several innovations to improve biocompatibility and ease of use. It is meant to be a good alternative for hospitals starting a new mechanical support program. The purpose of this study was to determine the short-term and 30-day *in vivo* performance of the Innovamedica VAD in healthy sheep.

II. MATERIALS AND METHODS

A. Animals

Eight healthy sheep, weighing between 55 and 91 kg, were used in this study. All sheep were quarantined for continuous observation. We provided humane animal care in compliance with applicable guidelines. The Institutional Animal Care and Use Committee approved all protocols used in the study.

B. Device Description

The system comprises the prototype device, inflow and outflow cannulae, the control consoles, and the transport unit as described below (fig.1).

This study was entirely performed and coordinated by the Cardiovascular Surgical Research Laboratory of the Texas Heart Institute under a grant from Innovamedica. The described VAD is a prototype developed for Vitalmex International by Innovamedica R&D in association with the Universidad Autonoma Metropolitana (UAM)-Iztapalapa. Dr. Sacristan, has several patents associated with this device. Ana L. Contreras is a graduate student at UAM and an engineering consultant for Innovamédica. None of the authors have any affiliation with Vitalmex International, assignee of all commercial rights.

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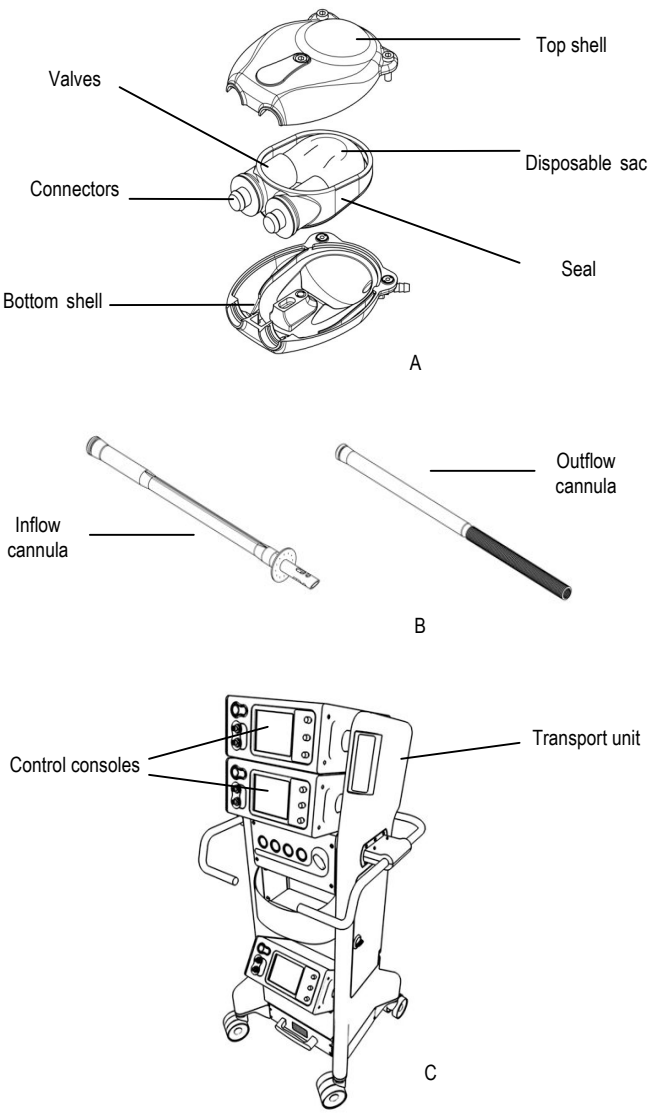

Figure 1 Component parts of the Innovamedica ventricular assist device (A) The artificial ventricle and disposable elements; (B) the inflow and outflow cannulae; and (C) the console unit.

The prototype device is a pulsatile pump unsynchronized to the natural heart rate. The artificial ventricle comprises two halves that seal hermetically to form a solid, hollow housing. This clamshell-like compartment contains the disposable components: unidirectional valves, metallic connectors, blood sac, and seal (Figure 1A). The valves and blood sac are made of elastic silicone. The hinge-less valves and flexible, elastic leaflets simulate the action of natural heart valves. The seal, made of a soft elastomer, is not in contact with blood and is used only to ensure an airtight fit of the pumping shell halves. The stainless steel connectors secure the connection between the valves and the cannulae. The sac is flexible and serves as a blood reservoir during systole and diastole. The inflow and outflow graft cannulae are depicted in Figure 1B.

The prototype control console consists of a pneumatic piston cylinder and valves. Together, these components provide air pulses by means of tubing connected to the artificial ventricle. The air pulses are managed by a control system that can be used to adjust parameters such as frequency, systolic/diastolic rate, ejected volume, and maximum diastolic and systolic pressures. The console contains sensors that auto-diagnose the cycle efficiency and turn on alarms for the user (Figure 1C).

The prototype transport unit consists of a hard structure with wheels that transport and protect the consoles during VAD operation. The unit can carry two operating consoles and one replacement console, and it provides space for the disposable components and accessories. In addition, the transport unit has electric and pneumatic connections, an option to use tank-pressurized oxygen, and an alternative battery supply for up to 4 hours (Figure 1C).

C. Short term Experimental Surgical Procedure

Six sheep were premedicated with glycopyrrolate (0.01-0.025mg/kg, subcutaneously) and ketamine (2-20mg/kg, intravenously) in order to induce anesthesia. Butorphanol (0.05-0.40mg/kg) was given as an analgesic. Once sedated, the sheep were moved to the operating room, and a triple lumen catheter was inserted into the right jugular vein to place a venous line. An orogastric tube was used to decompress the rumen. An endotracheal tube was placed to provide general anesthesia with isoflurane (0.5-3.0%) in O_2 (40-100%). To increase the duration of the blockade, pancuronium bromide (0.04-0.10 mg/kg) was administered intravenously.

We exposed the internal thoracic artery and placed a catheter to monitor arterial pressure. In addition, we exposed the left jugular vein and carotid artery to insert a Swan-Ganz catheter. A left thoracotomy was performed at the 5th intercostal space; the pericardium was incised from the apex to the pulmonary artery, and the

heart was suspended in pericardial cradle. The descending thoracic aorta was dissected for graft anastomosis and was partially clamped. A bolus of heparin was administered (3 mg/kg) to maintain the activated clotting time (ACT) above 300 seconds. The Dacron tip of the outflow graft cannula was sewn to the aorta with 4-0 Prolene sutures. An incision was made on the apex of the left ventricle to insert the inflow cannula, which was secured with a 2-0 interrupted Ticon pledgeted purse-string suture. The pump was primed with heparin/NaCl (10,000 units/1L) solution and attached to the inflow and outflow cannulae. The system was de-aired, and the aortic clamp was removed. A Transonic flow probe was connected to the outflow cannula, and the pump was started at t=0. The VAD drive unit was set up to provide optimal flow. Each sheep was maintained on left ventricular support for 6 hours and then humanely euthanized

Cardiac output, central venous pressure, and pulmonary capillary wedge pressure (PCWP) were measured via a Swan Ganz catheter. We measured cardiac output and central venous pressure at baseline and every 15 minutes thereafter. PCWP was measured every 30 minutes. A Transonic flow probe connected to the tubing was used to measure the VAD flow rate at baseline and every 15 minutes thereafter. Aortic pressure was continuously monitored via a pressure-filled catheter. We also monitored vascular and pulmonary resistance. Vital signs, including heart rate, respiratory function, temperature, and pH, were measured every 30 minutes.

To assess free plasma hemoglobin, we obtained blood samples at the following times: at least 3 days before surgery (control sample) at the same time as the preoperative laboratory studies (see below), on the experiment day before device implantation, 30 minutes after initiation of support, and every 60 minutes thereafter.

At least 3 days before surgery and during and after the procedure, we obtained blood samples to perform laboratory studies. The following variables were assessed: complete blood count, serum chemistry, serum electrolytes, reticulocyte count, prothrombin time, partial thromboplastin time, fibrinogen, haptoglobin, CKMB, plasma hemoglobin, serum magnesium and gamma glutamyltransferase. Arterial and venous blood gas samples were collected before the procedure and every 60 minutes throughout the study.

D. 30-day Experimental Implants

Two additional sheep (69 and 75 kg), were implanted with the Innovamedica LVAD using a similar surgical procedure as described above, to evaluate the device performance in a 30 day period. In these sheep, however we used a ventricular cannula with a 90^0 angled distal tip and both cannulae were connected transcutaneously to the VAD (see figures 2 and 3). The Swan-Ganz catheter was not used in these sheep, but we did use the transonic flow probe on the outflow cannula to measure the actual VAD output.

Control consoles operated on a fixed rate/variable ejection volume mode at 90 beats/min for the entire period. Anticoagulation consisted of Heparin for the first 48 hours as needed (Activated Coagulation Time was kept above 300s during the surgical implantation and then lowered to around 120s after surgery). After 72 hours, a combination of Warfarin/Aspirin was used for the rest of the experiment.

After 30 days, both sheep were euthanized and a necropsy performed to search for evidence of clot formation, infarcts, and other tissue damage.

III. RESULTS

A. Implantation Procedure

The average implantation time from cannulation to device pumping was 39 ± 7 minutes. The overall surgical time from first incision to pump start-up was 62 ± 7 minutes. There were no procedural-related events.

B. 6 hour Hemodynamic Performance

No device-related problems were observed in any sheep. The device sustained an overall mean blood flow of 4.4 ± 0.8 L/min, representing 86% of the total cardiac output**.** During ventricular support, mean arterial blood pressure, pulmonary artery pressure, and central venous pressure were maintained at normal levels: 76 ± 15 mmHg, 10 ± 6 mmHg, and 2 ± 2 mmHg, respectively.

C. 6 hour Hemolysis

The ACT was maintained at a mean of 650 ± 250 seconds during the study. The overall average concentration of plasma free hemoglobin was 5.11 ± 0.6 mg/dl compared with an average baseline value of 4.52 ± 0.7 mg/dl. The following variables decreased from baseline to study termination: hemoglobin, from 7.7 g/dL to 5.6 g/dL; hematocrit, from 24.3% to 17.2%; and fibrinogen, from 243 mg/dL to 151 mg/dL. Results from blood gas analysis and biochemical tests were within physiologic limits throughout the study.

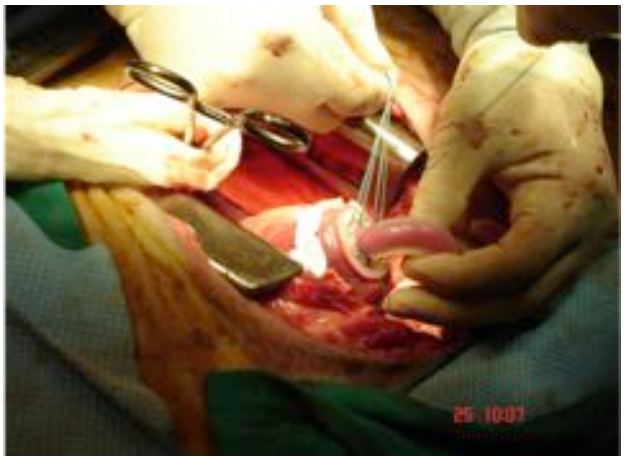

Figure 2 Ventricular cannula with a 90° angled distal tip.

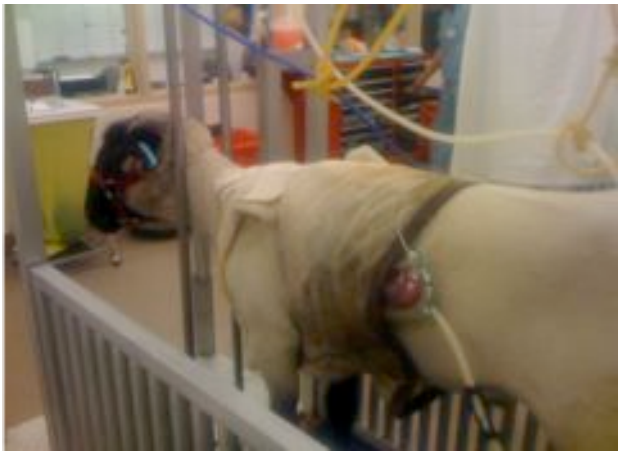

Figure 3 Sheep with implanted LVAD was kept with limited mobility in special pen for 30 days.

D. 30-day Performance

The devices were implanted in both sheep with a time from first incision to pump start-up of 72 minutes. Sheep 1 was re-operated after 8 hours because of excessive post-operative bleeding and received a blood transfusion. Sheep 2 had no post-operative complications. No other significant adverse events were seen for the remainder of the 30-day period.

Mean blood flow was 4 l/min ± 0.2, plasma free hemoglobin was 5.9 ± 4 mg/dl for the 30 day period excluding the first 48 hours. Warfarin/Aspirin anticoagulation was used after the first 72 hours with an average INR of 2.9 for the entire test period. Post-mortem showed no blood clots or any significant tissue damage to brain, lungs or kidneys, only a small infarct less than 3mm in diameter was found in the renal cortex of sheep 2.

IV. DISCUSSION

The in vitro performance of the Innovamedica VAD has been previously reported (6). In the present study, we assessed the short-term and 30-day *in vivo* performance of the Innovamedica VAD, a prototype pulsatile assist device. The device was easy to implant, requiring a short, safe de-airing process with its transparent rubber silicone ventricular sac. The device provided adequate hemodynamic support, and we saw no significant device-related adverse events during the experiments. Hemolysis was negligible during the test periods of support. Furthermore, we saw no evidence of thrombus formation in the device or any other biocompatibility problem.

In summary, the Innovamedica VAD prototype proved effective, reliable, and biocompatible in both the 6 hour and 30 day tests in sheep.

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