Clinical Experience with the Medos® Assist Device

G. Babatasi, M. Massetti, S. Bhoyroo, A. Khayat

Objective: A new pneumatic pulsatile ventricular device: the 60 ml Medos® Helmholtz Institut Aachen (HIA) was assessed for surgical congestive heart failure post cardiopulmonary by-pass (CBP) as a bridge to transplantation or recovery.

Design: The goal of our study was to report our clinical experience and to evaluate the thrombotic risk by biomarker prothrombin and microscopy of the blood contacting surfaces.

Setting: Heart care unit in University Hospital, first French experience with this device.

Patients: From November 1994 to December 1995, three patients required this artificial heart assist device for otherwise intractable heart failure. Mean age was 45 ± 6 years. Two were for temporary support leading to restoration of cardiac function including "weaning off" from CPB and the other was an acute cardiac decompensation before heart transplantation.

Main results: The device worked without any failure over a mean period of 18 ± 1 days (31-4) and generated a sufficient output between 5.4 to 6.3 liters. No activation of the procoagulatory system was detected during pumping. Measured blood parameters such as Prothrombin F_{1+2} (1.3 ± 0.2 nmol/l), antithrombin III activity (74 ± 2%), free haemoglobin indicated low mechanical haemolysis. The driving pressures for full-empty pump operations were significantly reduced, without exceeding 30 mmHg higher than the mean systolic pressure. After explantation, there were no signs of clotting in any cannulae, the interior blood contacting surfaces of the pump and the polyurethane valves.

Conclusion: The Medos® HIA-VAD is a blood pump with very low-risk of thrombo-embolic complications, a low-costable VAD with excellent hemodynamic properties.

(CVE. 1997; 2 (1): 16-18)

Key words: Mechanical circulatory support, blood pump, heart failure

Introduction

Ventricular assist devices (VAD) for uni or biventricular assistance have become a therapeutic tool for the treatment of endstage heart failure as a bridge to transplantation or recovery (1-5). VAD have so far been used only for a relatively small number of patients. VAD applications are mainly limited by various thromboembolic complications and by the high costs of commercial pump systems. Thromboembolic complications remain a major source of morbidity during and after application of VAD. Prothrombin fragment F_{1+2} is a group of molecular markers indicating the degree of thrombotic risk (6). The fragment F_{1+2} are cleaved from prothrombin during their activation by the factor Xa complex in order to form thrombin (7). Elevated F_{1+2} levels are routinely found in patients with disseminated intravascular coagulation, septicemia, and in the post-operative period (8, 9). Microscopy evaluation of the blood contacting surfaces of this pump was used to help for detecting sources of thromboembolism. During the last 10 years, a new pneumatically driven diaphragm-type blood pump has been developed at the Helmholtz-Institute in Aachen (HIA), which aims to overcome these limiting factors. A low-cost disposable VAD with appropriate hemodynamic properties may be used as a univentricular and a biventricular assist device during recovery, as well as a bridge to transplantation.

Material and Methods

The Medos® HIA-VAD Assist Device (60 cc)

This left-ventricular assist device operates as a heterotopic, extracorporeal pump propelling blood parallel to the natural heart and has been recently developed by the Helmholtz Institute in Aachen (HIA), Germany. Therefore the device is called the HIA ventricular assist device (HIA-VAD®). It is now manufactured by Medos GmbH, Stolberg, Germany. The pneumatically driven membrane-type pump is the result of computer-aided design, stress analysis, and in-vitro evaluation of the polyurethane three-leaflet valves. The completely transparent and smoothly working pump incorporates a multilayered diaphragm which separates the blood flow chamber from the pneumatic chamber of the pump. Two three-leaflet polyurethane valves are integrated into an in- and outflow connector. The pumping membrane is pneumatically driven by the console. The console can operate two pumps independently as synchroneously respectively asynchroneously to the heart beat. The geometry of the housing and the valves were developed separately and are manufactured by combined thermoforming and dip moulding out of polyurethane, producing a seamless diaphragm-housing junction. A special gluing technique provides a smooth transition between the parts, and silicon oil as a lubricant of the

Received January, 1997; accepted March 1997.

From the Department of Cardiovascular and Thoracic Surgery, University Hospital Caen, France.

Reprint requests to G. Babatasi, M. D., Department of Cardiovascular and Thoracic Surgery, University Hospital Caen, F-14033 Caen, France.

pump membrane leads to a completely transparent blood pump which can easily be de-aired. All surfaces in contact with blood are made of biocompatible polyurethane. The final design of the valves and outlet is conus shaped. This is based on findings obtained by in-vitro flow visualisation techniques and the finite-element method of stress analysis, where the conical design shows a superior performance especially in the open position. The new valve design made it possible to reduce driving pressures and vacuum, improve the filling behaviour, and avoid clot formation, as demonstrated during in-vivo testing (10-14). The pump volume can be varied by manufacturing different sizes. Currently there are five sizes at hand: 6, 10, 25, 60 and 80 ml. In our clinical experience the 60 ml version was used. Pumping was ECG triggered and was performed on a 1:1 basis. For right ventricular support stroke volumes are reduced by 10% for each size. Circulatory access for the left heart assist of 60 cm^3 was achieved transthoracically using a 14 mm right-angled silicone cannula (Berlin-heart-cannula) from the right border of the left atrium and a similar inflow cannula into the ascending aorta. Pump filling was achieved by gravity and gentile suction.

Blood Samples

Collection and processing of blood samples were done three times a day, via a central venous catheter. An aliquot of 10 ml was stored. The sample tubes were prefilled with 3.8% sodium citrate, the ratio of anticoagulant to blood was 1:9 (vol/vol) to measure coagulation parameters. For counting blood cells, Acid-citrique-dextrose (ACD) tubes were used and the blood samples drawn in the same way. Plasma fractions were obtained by centrifugation at 4°C during 10 minutes at 1600 g. Plasma samples for the F_{1+2} immunoassay were stored at -32°C before further evaluation for 2 weeks.

In all fresh samples of citrated plasma we measured PT, aPTT, fibrinogen with MLA Electra 1000 C (Medical Laboratory Automation, Inc., Baxter, Germany). The PT values were examined with Thromborel S reagent (Behring, Marburg, Germany), the aPTT with Actin FS (Baxter, Germany). Fibrinogen values were measured as derived fibrinogen performed during PT measurement. The ISI value for the Thromborel S was said to be as 1:1 by the manufacturer. Determination of the F_{1+2} in plasma was performed by using the commercially available kit Enzygnost F_{1+2} micro (Behring, Marburg, Germany). The reference range was 0.4-1.1 nmol/l, the intra assay coefficient of variation (CV) was 6%, the inter assay < 10%. Antithrombin III activity (AT III) was measured chromogenically (Behring, Marburg, Germany). In the ACD or EDTA anticoagulated whole blood samples the platelets were counted semiautomatically in a Sysmex M 2000 (Digitana, Hamburg, Germany). Haemoglobin, haematocrit, red and white blood cells were measured simultaneously in the same apparatus.

After explantation of the three ventricular assist devices for scanning electron microscopy, the pump system was carefully washed with normal saline and fixed in a buffered solution of 2.5% glutaraldehyde for 2 days. Specimens of all blood-contacting surfaces were then dehydrated by a graded series of ethanol, critical point dried with liquid CO_2, mounted on aluminium stubs and sputter-coated with gold. Observation and photography were performed using a Philips Scanning Electron Microscope.

Case Report 1

A 61 year old male patient with a history of angina and previous coronary bypass surgery 12 years before (saphenous graft on left descending artery) was admitted to the coronary unit for acute thoracic pain and abnormalities on ECG. At the angiocoronarography, the graft was severely stenosed with multiple stenosis on the LAD. Preoperative anterior myocardial infarction required coronary artery surgery using left internal thoracic artery in emergency was not sufficient enough to prevent left ventricular failure. Inotropic support and intraaortic balloon counterpulsation were necessary before implantation of a centrifugal pump (Biomedicus®). After 3 days of circulatory assistance with Biomedicus®, we decided to switch for a pulsatile cardiac assistance. The total length of assistance was 19 days which could be separated in three periods. The first fourth days with a total efficiency of the pulsatile left ventricule which pumped from the left atrium to the ascending aorta and used precoated cannulae with heparin. Postoperative continuous ventilatory support and hemofiltration were mandatory. Six hours postoperatively i.v. heparinisation was started. Partial thromboplastin times (aPTT) of 60-75 seconds were achieved, i.e. approximately double normal values. On the seventh day, hypoxemia appeared in relation with low cardiac index in spite of satisfactory left ventricular assist. It was due to restriction of aortic cannulae, the internal diameter of the cannulae (which was sufficient for centrifugal pump) was too small for pulsatile assistance and required implantation of a ten millimeters cannulae. During the next twelve days, the VAD was well-correlated with the cardiac index, providing pronounced unloading effect on left ventricle. Filling of the left ventricle was reduced as evidence by a reduction in filling pressure to 50-70% of its initial value. The last period of four days was characterized by occurence of a severe pulmonary infection associated with a septic shock. On the 19th day the patient died of multiorgan failure.

Case Report 2

A 42 years old man with unstable angina due to triple vessel disease and low rejection fraction required coronary artery bypass grafts including endarterectomy of the right coronary artery. A support by centrifugal pump was not sufficient to avoid left ventricular failure which indicated the implantation of the Medos® VAD-HIA. Blood loss during the first 24 hours were superior to 250 ml per hour and involved low levels of peripheral perfusion. The patient died on the 4th day with right ventricular failure and hepatic disorders, in spite of implantation of right assist device using another ventricle pumping from the right atrium to the pulmonary artery.

Case Report 3

A 35 years old man with a dilated cardiomyopathy was admitted in emergency for intractable left ventricular failure and required continuous ventilatory and inotropic support during 24 days. The hemodynamic situation was unstable and the patient was transferred in our intensive care unit for ventricular support. A Medos® HIA-VAD was implanted to assist the left ventricle. The driving pressures for full-empty pump operation were significantly reduced, and they did not exceed values 30 mmHg higher than the mean systolic pressure (60 ccm pump, 70 bpm). Cardiac index (thermo-dilution) was 2.4 $l/mn/m^2$ with systemic vascular resistance at 1100 U.I and pulmonary resistances at 200 U.I allowing to reduce inotropic drugs. On the 8th day, reoperation was required in emergency for acute compression of the right cavities with tamponade. During 19 days the Medos® HIA-VAD provided excellent hemodynamic situation, without thrombus formation. No opportunity of having heart transplant was available,

on account of scattered numbers of blood groups (AB). Unfortunately, the patient died after 31 days of left ventricular assistance from a continuous gastrointestinal bleeding in spite of surgery.

Results

The Medos-HIA LAD devices pumped 432 ± 2 hours with flow rates ranging from 5.4 to 6.3 liters per minute without any complication. Six hours postoperatively bloodloss due to I.V. heparinisation with an aPTT of 55-75 ± 10 seconds was about 450 ± 65 ml. Clinical signs of neurologic deficits due to thromboembolism could not be detected. The mean number of platelets decreased only slightly from 140 to 100 x 10^3 / mm^3 (mean 95 x 10^3 / mm^3) per ml thus substitution was not necessary. Perioperatively red and white cells, and AT III essentially revealed normal values. Mean level of AT III ranged 74% ± 2 (normal value, 85%). Mean fibrinogen level was 6.25 g/l (3.22-9.70), increasing in case of septic shock. Activation of coagulation indicated by prothrombin fragment F_{1+2} was at 1.3 ± 0.2 nmol/l (normal level of 1 nmol/l) during the whole pumping period and only increased when septic shock occured. No activation of coagulation by this type of pump could be found. Perioperative values of F_{1+2} were not estimated because of the usually occuring of the coagulation system.

Comments

For the first case reported, the major problem was the occurence, on 7th day, of hypoxaemia and low cardiac index due to restriction of inflow aortic cannulae (stay sutures providing excessive tension) requiring reoperation. Patient died of toxic shock syndrom after 19 days of mechanical support. Concerning the second patient, the delay between weaning of centrifugal pump to switch on pneumatic pulsatile device was excessive, so biventricular failure occured during this period with bad prognosis. For the last patient, there was no opportunity for having heart transplant during circulatory support, his blood group (AB) was uncommon. Clinical application of the Medos HIA-VAD was first reported by Eilers (14). The thromboembolic risk of the Medos® could be considered as very low under anticoagulative regimen. Macroscopically detectable signs of clotting were neither visible in the tubing nor in the pump, nor on the tricuspid polyurethane valves after clinical use. These findings are identical with findings of Bohle (15) in the polyurethane Abiomed 5000 assist device and in contrast with Bernhard (15, 16) who found fibrin coagula with thrombus formation on polyurethane blood sacks of the Pierce-Donachy pump. F_{1+2} showed low-levels with values inferior to 1 nmol/l. Depression of plasma levels is found in patients receiving heparin. F_{1+2} levels increased under condition of septicemia (17). Symptoms for disseminated intravascular coagulation could not be detected. No alterations of AT III levels, thrombocytes counts, fibrinogen concentration and global test parameters (aPTT, PT) were seen.

SEM surface analysis of the blood contacting polyurethane pumping chamber and both sides of the two polyurethane heart valves showed a fibrin layer without any platelet adhesions, in contrast with Abiomed device (15, 18). Post-mortem investigation did not show any thrombus formation around the insertion site of the cannulae inside the patient's left atrium and inner surface of the ascending aorta which have previously been described as a main source of thromboembolism. Filling of the left ventricle was reduced as evidenced by a reduction in filling pressure to 50-70% of its initial value (19).

We conclude that the Medos-HIA ventricular assist device is a safe, economic artificial blood pump with no measurable activation of coagulation, excellent surface characteristics and low risk of thrombo-embolic complications.

References

[1] De Bakey ME (1971) Left ventricular bypass pump for cardiac assistance. Clinical experience. Am J Cardiol 27: 3-12

[2] Golding LR, Jackobs G, Groves LK et al, (1982) Clinical results of mechanical support of the failing left ventricle. J Thorac Cardiovasc Surg 83: 597-601

[3] Pennock JL, Pierce WS, Wisman CB et al. (1983) Ann Surg 198: 469-478

[4] Pennington DG, Bernhard WF, Golding LR et al. (1985) Long-term follow-up of post-cardiotomy patients with profound cardiogenic shock salvaged by ventricular assist devices. Circulation 72 (suppl. 2): 216-226

[5] Bauer KA, Rosenberg RD (1987) The pathophysiology of the prethrombotic state in humans: insights gained from studies using markers of hemostatic system activation. Blood 70: 343-350

[6] Manucci PM, Tripodi A, Botasso M et al. (1992) Markers of procoagulant imbalance in patients with inherited thrombophilic syndromes. Thromb Haemostas 67: 200-202

[7] Jensen R, Ens GE (1991) Diagnostic application of thrombotic markers. Clin Hemostas Rev 5: 1-7

[8] Siemens HJ, Bruckner S, Hagelberg S, Wagner T (1993) Thrombophilia-changing levels of different parameters in the perioperative phase. Thromb Haemostas (Abstract) 69: 2932

[9] Knierbein B, Rosarius N, Reul H et al. (1990) New methods for the development of pneumatic displacement pumps for cardiac assist. Int J Artif Org 11: 751-759

[10] Rakhorst G, Hensens AG, Blanksma PK et al. (1992) Evaluation of a protocol for animal experiments with Helmholtz Left Ventricular Assist Devices. Cor Europ 4: 155-159

[11] Knierbein B, Rosarius N, Unger A, Reul H, Raug G (1992) CAD-design, stress analysis and in vitro evaluation of three leaflet blood-pump valves. J Biomed Eng 14: 275-286

[12] Rakhorst G, Hensens AG, Verkerke J et al. (1994) In-vivo evaluation of the HIA-VAD: a new German ventricular assist device. Thorac Cardiovasc Surgeon 42: 136-140

[13] Reul H, Taguchi K, Herold M et al. (1988) Comparative evaluation of disk and trileaflet valves in left-ventricular assist devices (LVAD). Int J Artif Org 11: 127-130

[14] Eilers R, Harbott P, Reul H et al. (1994) Design improvement of the HIA-VAD based on animal experiments. Int J Artif Organs 18: 473-478

[15] Bohle AS, Sievers HH, Bernhard A (1990) Scanning electron microscopy evaluation of the Abiomed 5000 ventricular support system after clinical biventricular assistance. Eur J Cardiothorac Surg 4: 671-674

[16] Schoen FJ, Bernhard WF, Khuri SF et al. (1982) Pathologic findings in postcardiotomy patients managed with a ventricular assist pump. Am J Surg 143: 508-513

[17] Estivals M, Pelzer H, Sie P et al. (1991) Prothrombin fragment F_{1+2}, thrombin-antithrombin III complexes and D-dimers in acute deep vein thrombosis: Effects of heparin treatment. Brit J Haematol 78: 421-424

[18] Schoen FJ, Palmer DC, Bernhard WF et al. (1986) Clinical temporary ventricular assist. J Thorac Cardiovasc Surg 92: 1071-1081

[19] Waldenberger FR, Pongo E, Meyns B, Flameng W (1995) Left-ventricular unloading with a new pulsatile assist device: the HIA-VAD System and its influence on myocardial stunning. Thorac Cardiovasc Surgeon 43: 313-319