Utilization of the Bentley BOS-CM50 Capillary Fiber Membrane Oxygenator with a Bio-Medicus Pump for Long-Term Right Ventricular Assist: A Case Report

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Abstract

Following six vessel coronary artery bypass surgery, a 67-year-old man developed acute hypoxia and severe pulmonary hypertension secondary to a protamine reaction. Right ventricular bypass with oxygenation was required using a Bio-Medicus pump and Bentley BOS-CM50 capillary fiber membrane oxygenator. This helped to lower the pulmonary artery pressure from 36 mmHg to 9 mmHg. Arterial blood gases were maintained with a pH of 7.35-7.50, pCO₂ 30-40 mmHg, and PO₂ 60-200 mmHg, and activated clotting times (ACT) were kept above 480 seconds. The oxygenator was used for 14 hours without complications and removed from the circuit when the patient’s mean pulmonary artery pressures were kept below 20 mmHg, and pO₂s above 60 mmHg with the patient supported on the ventilator. The patient was subsequently weaned off right ventricular bypass after 66 hours of support.

The Bentley CM50 capillary fiber membrane oxygenator was safely used for 14 hours, which was associated with a reduction in pulmonary hypertension in a patient recovering from a protamine reaction.

Introduction

Long-term extracorporeal membrane oxygenation (ECMO) has been used successfully since the late 1960s to treat patients with severe, reversible acute respiratory failure. Membrane oxygenators safely used for ECMO include the Bramson, Lande’ Edwards, and the Sci-Med Kolobow Lung. The latest advancement in membrane oxygenator technology has introduced the hollow fiber membrane oxygenator, which is designed so that blood flows through thousands of cylindrically shaped microporous, polypropylene fibers, while the ventilating gas surrounds each fiber. The fibers are “potted” on each end, creating a separate blood phase inside the fibers and a gas phase outside the fibers. The uniformly thin fibers provide a maximum blood film thickness of 100 microns.

The Bentley CM50 capillary fiber membrane oxygenator consists of two sections, a gas transfer module and a heat transfer module. The gas exchange portion contains 53,000 microporous capillary tubes enclosed in a polycarbonate housing which is encapsulated on both ends with polyurethane. It has an effective surface area of 5.3 m². The heat exchange portion consists of a single-piece of anodized aluminum tubing 58.5 inches in length, coiled around a sealed polyethylene core within a clear, fluted polycarbonate housing.

The hollow fiber membrane oxygenator has been widely accepted for routine open heart surgical procedures requiring cardiopulmonary bypass for less than six hours. Although isolated emergency cases have necessitated the long-term use of the hollow fiber oxygenator, its use for longer than twelve hours has not been widely advocated to date. This tacit recommendation is principally the result of a lack of clinical studies reporting its safety and performance during long-term use in human subjects. Recently in our institution, a patient developed severe acute respiratory failure and right heart failure secondary to a protamine reaction following cardiopulmonary bypass. Right heart assist with extracorporeal membrane oxygenation was required. This case report illustrates the safe use of the Bentley CM50 membrane oxygenator in the extracorporeal circuit for 14 hours in conjunction with right heart assist.

Case Report

A 67-year-old black male was admitted to West Jefferson General Hospital for elective coronary artery bypass grafting. His past medical history included chronic lung disease and hypertension. A cardiac...
catheterization revealed inferior wall hypokinesis and his global ejection fraction was 72%. Coronary angiograms showed that he had a 90% lesion of the left anterior descending artery and a total occlusion of a diagonal branch. He had a 90% lesion of his main circumflex artery prior to his first circumflex marginal branch and a 99% distal lesion. The right coronary artery was totally occluded distal to a right ventricular marginal branch which had a 60% lesion. His preoperative medications included nitrates, calcium channel blockers and theophylline.

Prior to the induction of anesthesia (while monitoring lines were being inserted), the patient exhibited a hypertensive episode with severe angina. Intravenous nitrates were administered to lower the blood pressure from 225/115 mmHg, and it was thought on the basis of evolving EKG changes that the patient was undergoing an acute myocardial infarction. Hypothermic cardiopulmonary bypass was quickly initiated, and the patient was cooled to 25°C. After 700 ml of crystalloid cardioplegia was infused into the aortic root, the septal myocardial temperature was 10.7 degrees centigrade. Six vessels were grafted with a cross clamp time of 64 minutes. Upon rewarming, the patient required Lidocaine and several attempts at cardioversion in order to obtain a normal rhythm. While the patient was being fully rewarmed, his pulmonary artery diastolic pressure was as high as 25 mmHg without ejection. After 166 minutes of cardiopulmonary bypass, several unsuccessful attempts were made to separate him from bypass. His systemic arterial pressures and cardiac output remained low and his pulmonary artery diastolic pressure was elevated. A Dopamine infusion was started, but despite this he could not maintain adequate systemic pressures.

At this time, a Kontron intra-aortic balloon was inserted and the patient was successfully separated from bypass. His mean arterial blood pressure was maintained at 65-75 mmHg with a cardiac output of 7.0–8.0 liters per minute, and a pulmonary artery diastolic pressure of 15 mmHg. Protamine was given and his arterial pressure became more labile. The pulmonary artery diastolic pressure began to increase to 20 mmHg and his cardiac output had decreased to 4.0 liters per minute. His mean arterial blood pressure was being maintained with Dopamine and Dobutamine.

As an attempt was made to close his chest, he developed ventricular tachycardia which required cardioversion. Lidocaine and Bretylium were given. Arterial blood gases showed acidosis and severe hypoxia with a pH of 7.30, pCO₂ 45–55 mmHg, and a pO₂ of 35–45 mmHg, on 100% FiO₂. Pulmonary artery diastolic pressures were severely elevated at 35–40 mmHg, however left atrial pressures were less than 10 mmHg and peak airway pressures remained unchanged (Figure 1). During this time right ventricular contraction was noted to be weakening. The picture was consistent with a pulmonary embolus, so cardiopulmonary bypass was re instituted and the pulmonary artery was opened. No clot was found, however with the re institution of bypass the pulmonary artery pressures were lowered and oxygenation and right ventricular contraction had improved.

An attempt was made to come off bypass, but despite trying an infusion of isoproterenol hydrochloride and epinephrine, the pulmonary artery pressures dramatically increased with a fall in arterial pO₂. In anticipation of long-term circulatory support the bypass

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Figure 1: The changes in pulmonary artery diastolic pressure (PAD), arterial pO₂, and peak inspiratory pressure (PIP) during the time period between the initial termination of cardiopulmonary bypass and the initiation of right heart assist.

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a Kontron Cardiovascular, Inc., Everett, MA 02149
The circuit was changed to a Bio-Medicus pump\(^b\), a Bentley capillary fiber membrane oxygenator\(^c\), a Pall Ultipore arterial blood filter\(^d\), and a Terumo venous reservoir\(^e\) (Figure 2). The circuit was primed with 2200 ml of Plasmalyte A and 5,000 units of beef lung heparin.

Poor right ventricular contractility and pulmonary hypertension in addition to normal left atrial pressures indicated that we were now dealing with right heart failure and a decision was made to bypass the right ventricle. Following placement of the aortic cannula into the pulmonary artery a dramatic decrease in the pulmonary artery pressures were observed. Quite possibly the severe pulmonary hypertension caused right ventricular failure. When the pulmonary system was perfused with oxygenated blood, there was an associated decrease in the pulmonary vascular resistance resulting in reduced right ventricular end diastolic dimensions. After the initiation of right ventricular assist, with a pump flow of 4.0 liters per minute, and Fi\(_0\_2\) of 100% and a sweep gas of 4.5 liters per minute the systemic pressures were maintained at 70–80 mmHg, and left atrial pressures were 10–15 mmHg.

While on right ventricular assist with extracorporeal membrane oxygenation, activated clotting times (ACT), hematocrit and arterial blood gases were measured hourly. Arterial blood gases were drawn from the left radial line and were maintained at a pH 7.35–7.50, pCO\(_2\) 30–40 mmHg, and pO\(_2\) 60–200 mmHg. ACTs were kept above 480 seconds, and the hematocrit between 25 and 30. During the next several hours the Fi\(_0\_2\) of the membrane oxygenator was weaned from 100% to 21% and sweep gas from six liters per minute to one liter per minute. Simultaneously, the patient’s ventilator settings were altered to maintain the desired blood gas values. After 14 hours of extracorporeal membrane oxygenation, mean pulmonary artery pressures remained less than 20 mmHg and the patient was able to maintain adequate blood gases supported only on the ventilator (Table 1). At this time the patient was switched over to another circuit eliminating the membrane oxygenator.

The patient was then taken to the Surgical Care Unit where he remained supported by the intra-aortic balloon pump and the right heart assist pump for an additional 52 hours. With the membrane oxygenator absent from the circuit, ACTs were allowed to fall to 200 seconds. Dye dilution cardiac outputs were performed to assess right ventricular performance with the patient on and intermittently off the assist pump. On the third postoperative day, cardiac outputs and optimal systemic arterial and left atrial pressures indicated that this was adequate recovery time for the right ventricle. The patient was returned to the operating room and successfully separated from the assist pump.

After the assist pump was removed, an unsuccessful attempt was made to close the patient’s chest. On this attempt the pO\(_2\) dropped to 40 mmHg with an Fi\(_0\_2\) of 100% on the ventilator, so it was decided not to close the chest at this time. The intra-aortic balloon was removed at day 5 and the chest was closed postoperative day 18. The patient was subsequently weaned from the ventilator and discharged from the hospital after a prolonged convalescence. He has been seen as an outpatient and is doing well.

**Discussion**

Adverse effects of heparin neutralization with protamine sulfate vary from mild hypotension to severe cardiovascular collapse, including marked systemic hypotension, a reduction in cardiac output and arterial oxygen tension and a profound increase in pulmonary vascular resistance.\(^{19–23}\) The mechanisms responsible for these side-effects are thought to be either by a direct drug induced mechanism (non-immunologic), or they are stimulated by an allergic reaction to the drug (immune-mediated anaphylaxis).\(^{24–28}\)

In reviewing the sequence of events elicited by this patient, he initially exhibited signs of mild left ventricular failure which was believed to be a result of a
Table 1
Values during Weaning of the Membrane Oxygenator

<table>
<thead>
<tr>
<th>TIME</th>
<th>ARTERIAL BLOOD GASES</th>
<th>BENTLEY CM50</th>
<th>VENTILATOR</th>
</tr>
</thead>
<tbody>
<tr>
<td>(hours)</td>
<td>pO2 (torr)</td>
<td>pCO2 (torr)</td>
<td>pH</td>
</tr>
<tr>
<td>PRE</td>
<td>38</td>
<td>28</td>
<td>7.49</td>
</tr>
<tr>
<td>2</td>
<td>343</td>
<td>31</td>
<td>7.44</td>
</tr>
<tr>
<td>4</td>
<td>199</td>
<td>30</td>
<td>7.44</td>
</tr>
<tr>
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<td>229</td>
<td>30</td>
<td>7.48</td>
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<tr>
<td>8</td>
<td>271</td>
<td>30</td>
<td>7.48</td>
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<tr>
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<td>29</td>
<td>7.49</td>
</tr>
<tr>
<td>12</td>
<td>82</td>
<td>29</td>
<td>7.52</td>
</tr>
<tr>
<td>*14</td>
<td>94</td>
<td>33</td>
<td>7.47</td>
</tr>
</tbody>
</table>

* After 14 hours, the membrane oxygenator was eliminated from the right heart assist circuit.

During perioperative antero-septal infarction. He was stabilized with inotropic support and an intra-aortic balloon pump, however his subsequent hemodynamic instability has been attributed to a protamine reaction. The severe hypoxia and pulmonary hypertension produced by this reaction combined with the antero-septal infarction impaired right ventricular performance requiring right heart assist and extracorporeal membrane oxygenation. Recent medical literature has supported the successful use of mechanical circulatory assist for the treatment of acute right heart failure. \(^{29,30}\)

One of our major concerns was to oxygenate the blood since the patient was severely hypoxic. Serendipitously, we discovered that perfusion of the pulmonary artery with oxygenated blood lowered the pulmonary vascular resistance. In this acute situation, the availability of a membrane oxygenator was limited to the Bentley CM50. Several evaluations of the polypropylene hollow fiber membrane oxygenator indicated satisfactory performance of transfer of oxygen during prolonged extracorporeal oxygenation in humans and calves. \(^{31-33}\)

Since this was our first experience with a hollow fiber oxygenator for ECMO, anticoagulation was a special consideration. Ward and associates\(^{34}\) have previously evaluated the performance efficiency of clinical membrane oxygenators (Sci-Med Kolobow lung, Lande' Edwards, and General Electric) in calves. Their findings of diminished oxygenator performance for each design during ECMO was related to thrombogenesis and/or adverse mechanical effects. Thrombus formations in all three oxygenators were significantly reduced with heparin infusions. Mechanical defects were related to alterations in the configuration of the membrane lung, maldistributions of ventilation and perfusion and excessive condensation. In order to avoid thrombogenesis within the capillary fibers, we kept our ACTs above 480 seconds with intermittent injections of beef lung heparin (2500 to 5000 units). We did not visualize any evidence of thrombus formation or excessive condensation within the oxygenator. We did not perform a definitive evaluation of the gas transfer efficiency of the Bentley membrane due to the fact that this case was not an experimental study. Blood sampling was kept to a minimum, however the arterial pO\(_2\)s that were sampled from the patient's left radial line indicated that adequate oxygenation was accomplished. Our patient did not appear to suffer any complications from the Bentley CM50 and we did not encounter any difficulties in using it for 14 hours with adequate anticoagulation.

In appropriate situations we recommend further clinical trials using hollow fiber membrane oxygenators for prolonged extracorporeal oxygenation, to evaluate their efficiency and hematological effects. Although studies have been documented using con-
ventional membrane oxygenators ECMO,1-16 we have experienced favorable results using a hollow fiber membrane. Its temporary support in this case changed what would otherwise have been a catastrophic event into an acceptable outcome for our patient.

References


Questions from the Audience

Question—David Mills: I was curious as to whether this patient had any history of diabetes and whether the patient perhaps, at some point, received some NPH insulin, which has been indicted for sensitization to protamine reaction?
Answer: No, sir, the patient had no history of diabetes or prior administration of protamine zinc insulin or NPH insulin. I don’t believe he had prior exposure to protamine, either.

Question—Bob Emerson: What was the patient’s pre-op crit?
Answer: Sorry, I do not have that information available.

Question—Bob Emerson: I was just wondering if it might have been elevated. You mentioned that when you instituted the extracorporeal bypass at the end of the changeover that you ran your hematocrits down around 25. Did you try raising that hematocrit at any time during the 14 hours?
Answer: No, sir, we tried to keep it between 25 and 30, but we had difficulty getting it that high.

Question—Bret Smith: How did you administer the protamine? Was it drip or bollus—and had you changed your techniques since this event?
Answer: We usually give a small bollus to start with and see how the patient reacts. Then we give the rest of the dose. That’s how we gave it in this patient. We normally give Tagamet to our patients upon rewarming and we give benadryl (50mg.) before the protamine. And the only thing that we do more now is that we give the benadryl, which we hadn’t done previously.

Question—Bret Smith: What’s your time frame? Do you break it up into milligrams per minute or any other timing event? Do you try to get it in before a certain time?
Answer: We don’t have a specific time period. We usually do it over the course of about 15 minutes.

Question—Charlene Roher: Why did you decide to put an arterial filter in your circuit?
Answer: Initially we had decided to go to another circuit with the Bentley membrane. Our custom packs have arterial filters, and we also wanted to have a filter with an oxygenator online. We thought that would be important.

Question—For ECMO, we have used Terumos for a long term when we did not have anything else, and we still do not put an arterial filter in so that we could run our ACTs about 280 to 300. Do you happen to know what your platelet counts were?
Answer: Yes, I do. Prebypass platelet count was 346,000, post bypass 104,000. From then on it dropped to 98,000.

Question—They said that 14 hours—you probably wouldn’t have seen that much. But we had a lot of kids on for 60 hours, 6 days and you wouldn’t want an arterial line filter in that. You would have absolutely no platelets left.