Pump-induced haemolysis: a comparison of short-term ventricular assist devices

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Centrifugal pumps are superior to roller pumps for extended support durations in terms of pump-induced haemolysis. In this study, we evaluated the commonly used Biomedicus BP 50 and compared it with the Jostra Rotaflow and a standard roller pump in an in vitro test circuit. Each circuit was run for a six-day period and repeated five times. Plasma haemoglobin values showed the roller pump to become more haemolytic than the Biomedicus ($p = 0.022$) and the Rotaflow. A statistically significant difference between the Biomedicus and the Rotaflow was observed on day six of the trial ($p = 0.016$), with the Rotaflow showing lower levels of haemolysis than the Biomedicus. These results support the use of the new generation centrifugal pump, the Rotaflow, as a suitable device for short-term ventricular assist.

Introduction

Haemolysis, and its associated effects, remains one of the most common complications occurring in children undergoing Extracorporeal Life Support (ECLS). The Extracorporeal Life Support Organisation’s (ELSO) 2003 July Summary reports an incidence of haemolysis (as indicated by an elevated plasma-free haemoglobin $> 0.5$ g/dL) to be in the order of 9.3% of all cardiac patients supported. Many authors have highlighted the method of blood propulsion as a major contributor to this haemolysis. McDonald et al. showed that change-out of the pump-head alone, in a series of 48 ECMO patients, was able to reduce plasma-free haemoglobin levels back to baseline values. This group used the Biomedicus (Biomedicus - Medtronic Biomedicus, Inc., Eden Prairie, MN, USA) BP50 (paediatric version – 50 mL volume and two internal cones) and the mean duration of support with the original pump-head was 91.9 hours.

Previously, we have described a study comparing pump-induced haemolysis in the constrained vortex centrifugal pump with the roller pump. This earlier work was one of the first studies to demonstrate clearly the improved blood handling characteristics of centrifugal pumps in the long-term ECLS setting. This earlier study investigated the Biomedicus, which has since been widely used clinically and for centrifugal pump studies.

In the ensuing years, numerous variations in the design of the centrifugal pump have been put forward. Reul recently described six different centrifugal pumps currently in clinical use. A new design that has become clinically available is the Rotaflow (Jostra Medizintechnik AG, Hirrlingen, Germany). This pump uses a shrouded impeller and has a low-friction, blood-immersed, monopivot. In theory, this pump should provide superior blood handling properties in terms of pump-induced haemolysis over the more traditional shaft–seal design found in the Biomedicus and other centrifugal pumps.

To confirm the choice of centrifugal pump for our ECLS program, we performed an in vitro laboratory bench test evaluating haemolysis produced by a roller pump (COBE Cardiovascular, Arvada, CO, USA), a constrained vortex centrifugal pump (Biomedicus) and a shrouded impeller centrifugal pump (Rotaflow).

Materials and method

The experimental set-up consisted of three pumps: the Biomedicus BP-50 constrained vortex centrifugal pump, the Rotaflow shrouded impeller centrifugal pump and a standard roller pump.

An in vitro circuit was constructed for each of the three pumps that closely mimicked our clinical ventricular assist device (VAD) circuit, used with patients requiring up to 2 L/min of support. Each
circuit was similar in tubing length, connectors and sampling sites. The circuit loop consisted of a pump-head, ¼ inch PVC tubing, inlet and outlet pressure monitoring sites and a 1-L blood bag with sampling ports, which acted as the circuit reservoir. In the case of the roller pump, the pump-head was replaced by a length of ¼ inch silicone replacement tubing (Plastraon, City of Industry, CA, USA) (Figure 1).

The circuits were primed with a fresh unit of citrated whole human bank blood. The unit was weighed to determine its volume and then transferred to a 1-L blood bag. Plasmalyte 148 (Baxter Healthcare, NSW, Australia) was used to make up the remaining volume in the bag to 950 mL and to this 500 mg of Flucloxacillin and 15 mmol of sodium bicarbonate were added. Before the Plasmalyte 148 was added to the citrated whole blood it was oxygenated and then the combined blood mixture solution was gently agitated by hand. Once mixed, blood gas analysis was performed to confirm a sample that would closely match with normal biochemistry, which, it was postulated, would optimize red blood cell life. Three hundred millilitres of the blood mixture were then used to prime each of the three circuits, with the remaining volume being used as the control sample, unexposed to any of the three circuits. Any air in the circuit was then vented to minimize the blood–air interface.

Trial conditions were established using the Bio- medicus as the reference pump. These conditions consisted of an inlet line pressure range of −15 to −20 mmHg, outlet line pressure of 130–140 mmHg and a flow rate of 700 mL/min. These parameters were used following analysis of our patient VAD
database which showed that the average flow rate used in 52 patients who utilized the Biomedicus BP 50 for support was 720 mL/min and the average outlet pressure was 135 mmHg. A more negative pressure than the database average (−14 mmHg) was chosen, as previous studies have shown minimal haemolysis when the inlet pressure is maintained more positive than −15 mmHg. As the aim of our study was to observe haemolysis, the upper value of our database was used as the negative inlet pressure for this study. The inlet pressure was obtained by adjusting the height of the blood reservoir relative to the height of the pump-head. Outlet line pressure was adjusted by placing variable occlusion clamps on the outlet tubing. It has been noted that this method of obtaining outlet resistance may, in itself, cause increased turbulence and result in greater haemolysis, but these clamps were chosen as they were able to produce a reliable afterload and any contribution to haemolysis should be consistent across all three circuits.

Once trial conditions were established in the Biomedicus circuit, flow was established in the Rotaflow and roller pump circuits with the same reservoir height and outlet occlusion as for the Biomedicus circuit.

Flow rates were measured by a Biomedicus in-line flow probe for both centrifugal pumps and directly from the roller pump that was precalibrated using a Biomedicus in-line flow probe. Tubing occlusion for the roller pump was set using the method outlined by Mora. For each circuit, flow and pressure drift were checked and recalibrated at each sampling period. All experiments were conducted at room temperature.

Blood samples were taken from the three circuits as well as from the control bag at the same time daily. Each trial was performed for a six-day period and repeated five times. Blood samples were drawn into 5 mL ethylene-diamine-tetra-acetic acid (EDTA) tubes and then plasma was obtained by centrifugation. The plasma was frozen and then analysed for plasma-free haemoglobin (PHb) in a batch lot at a later time. Blood gas analysis was performed using a Ciba Corning blood gas analyser (Ciba Corning Diagnostics, Medfield, MA, USA), and PHb analysis performed by a Beckman DU-70 Spectrophotometer (Beckman Coulter, Fullerton, CA, USA), according to the method described by Burtis and Ashwood.

**Table 1 In vitro comparison; roller pump versus Biomedicus versus Rotaflow.** Plasma haemoglobin results g/dL.

<table>
<thead>
<tr>
<th>Pump</th>
<th>Day</th>
<th>Range</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Roller (n = 5)</td>
<td>1</td>
<td>0.05–0.63</td>
<td>0.27</td>
<td>0.24</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>0.20–0.75</td>
<td>0.43</td>
<td>0.28</td>
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<tr>
<td></td>
<td>3</td>
<td>0.32–2.02</td>
<td>0.85</td>
<td>0.69</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>0.42–2.54</td>
<td>1.10</td>
<td>0.85</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>0.40–3.14</td>
<td>1.39</td>
<td>1.09</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>0.53–3.66</td>
<td>1.76</td>
<td>1.25</td>
</tr>
<tr>
<td>Biomedicus (n = 5)</td>
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<td>0.12</td>
<td>0.06</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>0.05–0.23</td>
<td>0.17</td>
<td>0.07</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>0.07–0.39</td>
<td>0.26</td>
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<tr>
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<td>0.32</td>
<td>0.17</td>
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<tr>
<td></td>
<td>5</td>
<td>0.20–0.56</td>
<td>0.42</td>
<td>0.16</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>0.37–0.69</td>
<td>0.60</td>
<td>0.13</td>
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<tr>
<td>Rotaflow (n = 5)</td>
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<td>0.04–0.24</td>
<td>0.12</td>
<td>0.08</td>
</tr>
<tr>
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<td>2</td>
<td>0.05–0.32</td>
<td>0.16</td>
<td>0.11</td>
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<tr>
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<td>0.18</td>
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<td>0.30</td>
<td>0.19</td>
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</table>

**Statistical analysis**

A one-way analysis of variance (ANOVA) on natural log transformed data of plasma-free haemoglobin measurements was performed (Stata Quest 4.0, Stata Corporation, College Station, TX, USA). The Mann–Whitney U-test was then used to determine at what day a difference between the nontransformed data of the Biomedicus and Rotaflow pumps occurred. A probability value less than 0.05 was considered significant.
Results

Mean and standard deviation results of PHb values over the five weeks of the trial were compared for the three pump groups (Table 1). For the statistical analysis, PHb values for the control sample were deducted from the daily results of the three pump groups. The geometric mean for PHb values was then plotted against sample day (Figure 2). It can be seen that there is a trend for the roller pump becoming more haemolytic than both centrifugal pumps following only 24 hours of circulation, with levels continuing to rise over the course of the trial (p = 0.015). For the comparison between the Biomedicus and Rotaflow pumps only, ANOVA calculations on log transformed data showed a difference between the two groups with p = 0.038. (The Mann–Whitney U-test determined this difference to be significant on day six of the trial [p = 0.016].) Three of the five trial periods were extended beyond six sampling days with subsequent days showing a more pronounced difference between the Biomedicus and the Rotaflow, mean PHb 0.82 and 0.27 g/dL, respectively.

Discussion

Our findings firstly support our previous work and clinical experience, as well as those by other authors. In our earlier study, we showed the constrained vortex pump (Biomedicus) to be superior to the roller pump in terms of haemolysis produced over a five-day period. The results from this study support these findings, with both the Biomedicus and Rotaflow proving to be less haemolytic over a six-day period. In the clinical setting, it is known that centrifugal pumps are preload and afterload dependent and that changes in pump inflow can produce increased levels of shear stress and resulting haemolysis. As described previously, with appropriate management of the VAD or ECMO circuit, including the monitoring of pump inlet pressure, these deleterious effects can be minimized.

Our clinical approach to patients being supported by the Biomedicus had been to electively change the pump-head in the VAD circuit after a five-day period. This protocol had been adapted over some years of clinical experience and the observation that PHb values were seen to rise to levels considered to cause haemoglobinuria and renal damage at day five of support, as well as an increased likelihood of mechanical failure. This time-frame was also consistent with results from other studies. Since we have used the Rotaflow in the clinical setting, we have found PHb levels to be lower and have, thus, altered our policy on pump-head change-out such that there are no elective pump-head changes. PHb measurements are undertaken daily and careful examination of the patient circuit for visible signs of thrombus is performed. Sequential PHb readings greater than 0.6 g/dL generally will require some form of circuit component change-out. In 27 cases since May 2000, which utilized the Rotaflow as their support device, we have not had to change a pump-head due to an isolated rise in PHb or mechanical failure. Six pump-heads have been changed due to fibrin deposition or visible circuit clots. We feel that the results of this trial confirm our previous policy of electively changing the pump-head at day five of support and also the decision to change to the Rotaflow as our device of choice.

Our results are consistent with other studies which compare the roller pump and various centrifugal pumps; however, this study is the first to show results over an extended circulation period, which is perhaps more reflective of the clinical ECLS setting than the routine cardiopulmonary bypass (CPB) environment. The difference in results observed between the Biomedicus and Rotaflow could be due to a number of factors. Mendler and colleagues summarize many of the proposed mechanisms for the differences between the two pumps. The Biomedicus belongs to a class of centrifugal pumps that have a frontal magnetic drive. This mechanism of drive coupling necessitates a solid drive axle and a heavy-duty bearing that appears to be the basis of much of the pump-induced haemolysis. The nature of the solid shaft axle and bearing leads to a high level of heat generation and regions of poor blood washout. Together, these factors potentiate both clot formation and haemolysis. In contrast, the Rotaflow design utilizes a simple and very stable radial magnetic suspension that eliminates the need for a large drive shaft. In place of the shaft, a shrouded impeller sits on top of a sapphire monopivot bearing. This bearing is continually blood flushed, diminishing excessive heat generation, stagnant blood zones and reducing areas of high shear stress. It is these properties which may lead to improved blood handling and lower levels of pump-induced haemolysis as was evident in this trial.

This study has utilized a model of a VAD incorporating commonly used blood pumps. We have shown that for short-term use, such as the normal CPB setting, all three pumps produce acceptable levels of haemolysis, but when support duration is extended, the Rotaflow is less haemolytic and
less likely to fail. Thus, in our opinion, the Rotaflow is a better device for extended support.

Acknowledgements

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References

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