Study Results of a New Centrifugal Pump for Medical Perfusion Complex to Restore and Maintain the Viability of the Isolated Donor Liver

Vyacheslav Valentinovich Kharlamov, Alexandr Vasiljevich Shumilov, Konstantin Yurivich Senchik, Galina Sergeevna Kireeva, Sergey Alexandrovich Nikitin and Nikolay Anatoljevich Gryaznov

Department of Medical Equipment, Central Research Institute of Robotics and Technical Cybernetics, Saint-Petersburg, Russian Federation; sl@rtc.ru; shumilovalexandr@mail.ru; k-yurjivich@mail.ru; galinakireyeva@mail.ru; s.nikitin@rtc.ru; gna@rtc.ru

Abstract

Objectives: The article deals with experimental studies of original centrifugal pump developed in the Central Research Institute of Robotics and Technical Cybernetics (Saint-Petersburg, Russia) and designed for the use in apparatus for machine perfusion of the donor liver. Methods: In 4 series of experiments the traumatic effect of the pump on blood cells and changes in certain parameters during the perfusion with donor blood were studied. Blood samples were taken before the perfusion and at 60, 120, 240 minutes of the perfusion. Blood samples were analyzed using spectrophotometer and hematologic analyzer. A study of pressure-flow characteristics of the centrifugal pump incorporated into the developed apparatus for machine perfusion with arterial and venous lines was also performed. Findings: After 4 hours of donor blood circulation in the closed circuit by means of the studied pump there were no significant changes in blood parameters except for increase in free hemoglobin concentration which was comparable to what happens during the perfusion with a roller pump. The centrifugal pump provides pressure-flow characteristics required for perfusion of donor liver both in arterial and venous lines. In the operating area of hydrodynamic characteristics of the pump incorporated into the apparatus for machine perfusion of donor liver the fluid pressure in the arterial and venous lines reaches 2.7 and 2.3 m, respectively. Improvements: In experimental study it was shown that original centrifugal pump is safe and effective in terms of blood perfusion and it looks promising for the use in the apparatus for machine perfusion of the donor liver.

Keywords: Blood Trauma, Centrifugal Pump, Liver Transplant, Machine Perfusion, Peristaltic Pump, Pressure-Flow Characteristics

1. Introduction

How to keep donor liver viable for its further successful transplant to a recipient is one of the most urgent problems in transplantology. In liver transplantation process there is a retention period when after collection from a donor a liver is stored and transported outside the natural environment of human body. The duration of this period depends on many factors related to the donor, recipient and logistics of the transplant process, and it can be from 6 to 15 hours1. During this time, the liver is cut from the life support mechanisms such as blood circulation and oxygenation, and accordingly, there is organ ischemic injury. In order to minimize this damage liver machine perfusion is used providing circulation of the preservative solution through the liver microcirculation2. Machine perfusion provides thorough washing of blood cells required for optimal and uniform liver perfusion, and supplies the organ with oxygen. Moreover residual blood cells could cause inflammatory reaction and induce immune response against the donor cells3. The main element of perfusion machines is a perfusion pump. A roller pump is still used as a common pump in these machines but it cannot be considered as an optimal choice for this

*Author for correspondence
purpose due to several reasons. Specialists in the Central Research Institute of Robotics and technical cybernetics have been developing an apparatus for normothermic machine perfusion of the donor liver. The key element of this apparatus is an original centrifugal pump created in the same. The article presents the results of experimental studies of this pump.

2. Materials and Methods

Experiments were performed with a centrifugal perfusion pump which is to be included into apparatus for normothermic machine perfusion of the donor liver Figure 1. The traumatic effect of the pump on blood cells and changes in some other blood parameters during the perfusion were studied. To do so a perfusion circuit was formed and filled with donor blood. Standard perfusion circuit (pump segment made of silicone rubber and polyvinyl chloride with a diameter of 8 mm, perfusion line with a diameter of 8 mm) was connected to the studied pump. Centrifugal nozzle was set on the pump. The circuit was filled with donor blood (hemoglobin - 120 g/l, hematocrit - 45%, temperature - 37±1°C). Circulation speed was 500 ml/min, duration of circulation was 4 hours. Normothermia was maintained by means of the water bath where a free loop of the perfusion line was placed. Right before the circulation, at 60, 120 and 240 minutes of the perfusion blood samples (5 ml) were taken from the circuit for the analysis. Perfusion was stopped after 4 hours of blood circulation. Analysis of blood samples was performed right after the sampling using spectrophotometer SS1207 (LEKI Instruments, Russia) and hematologic analyzer MicroCC-20 Plus (HTI, USA). There were four series of the experiments.

The authors also performed a study of pressure-flow characteristics of the centrifugal pump incorporated into the developed apparatus for machine perfusion with arterial and venous lines.

The results of the study were statistically processed using Microsoft Excel, SPSS Statistics (IBM, USA).

3. Results

The results of studying traumatic effect of the pump on blood cells and changes in certain blood parameters are given in Table 1. It was found that there was a significant increase in free hemoglobin concentration by the end of the perfusion time (p<0.005) with the value of this parameter at 4 hours of the perfusion with centrifugal pump being 0.11±0.04 g/l. This value does not exceed the value reported for roller pumps (0.14±0.05 g/l). Results of study of pressure-flow characteristics of the centrifugal pump are presented in Table 2 and Figures 2-3. It was established that in the operating area of hydrodynamic characteristics of the pump incorporated into the apparatus for machine perfusion of donor liver the fluid pressure in the arterial and venous lines reaches 2.7 and 2.3 m, respectively.

4. Discussion

Roller pumps have been commonly used for bypass procedures for the last 50 years. However, recently their popularity has started decreasing due to evolution of the systems based on the centrifugal pumps. The main disadvantage of roller pumps is the fact that the degree of occlusion of a peristaltic pump can be adjusted only by increasing/decreasing the compression rollers of perfusion lines, and the degree of compression is a critical parameter. Too strong compression triggers hemolysis of the perfused blood and causes rapid wear of perfusion lines, while too poor occlusion may also cause hemolysis and, more importantly, complicates output control.
Table 1. Changes in blood parameters values during perfusion with the centrifugal pump

| Parameters                                | Values before perfusion | Values during perfusion |
|-------------------------------------------|-------------------------|-------------------------|
|                                           |                         | 1 hour                 | 2 hours                 | 4 hours                 |
| Red blood cells $10^{12}$/l               | 3.9±0.5                 | 3.9±0.6                 | 3.8±1.2                 | 3.7±0.3                 |
| Leucocytes $10^9$/l                       | 5.8±1.2                 | 6.0±1.4                 | 6.1±1.0                 | 5.8±0.9                 |
| Trombocytes $10^9$/l                      | 250±3.5                 | 220±4.2                 | 215±12.5                | 203±15.4                |
| Erythrocyte sedimentation rate, mm/h      | 3.4±1.2                 | 3.5±0.5                 | 3.7±0.4                 | 3.8±1.1                 |
| Total protein, g/l                       | 67.1±2.3                | 68.3±2.5                | 66.3±2.4                | 67.1±3.4                |
| Fibrinogen, g/l                          | 2.3±0.5                 | 2.2±0.3                 | 2.1±0.9                 | 2.0±0.4                 |
| Osmotic resistance of erythrocytes        | 0.89±0.11               | 0.90±0.12               | 0.88±0.11               | 0.89±0.13               |
| Indicator of red blood cells deformability, % | 92.2±1.3               | 94.2±1.1               | 93.2±0.9               | 93.8±0.8               |
| Free hemoglobin, g/l                      | 0.11±0.05               | 0.11±0.05               | 0.12±0.06               | 0.11±0.04               |
| $K^+$ of blood, mol/l                     | 6.5±1.1                 | 6.6±1.3                 | 6.4±1.2                 | 6.5±1.2                 |
| Hemoglobin of the red blood cells, g/l    | 126.5±2.8               | 128.7±2.5               | 127.6±3.5               | 129.7±3.5               |

Table 2. Pressure-flow characteristics of the centrifugal pump incorporated into the apparatus for machine perfusion of the donor liver

| Arterial line | Venous line |
|---------------|-------------|
| Consumption, l/min | Pressure, m | Consumption, l/min | Pressure, m |
| 0.05          | 0.3         | 0.5              | 0.2          |
| 0.1           | 1.0         | 0.7              | 0.7          |
| 0.2           | 1.65        | 0.9              | 1.1          |
| 0.3           | 2.25        | 1.1              | 1.65         |
| 0.4           | 2.6         | 1.3              | 1.8          |
| 0.5           | 2.7         | 1.5              | 2.1          |
|               | 1.7         | 2.3              |              |

Here are some other disadvantages associated with use of roller pumps: 

- Changes (disturbances) in the calibration;
- Damage / wear of perfusion lines;
- Power loss;
- Ability to pump significant amounts of air.

Centrifugal pumps were introduced into medical practice in 1976, and since then they started to replace roller pumps in terms of cardiopulmonary bypass. They are also used for mechanical support of circulation, e.g. as an auxiliary ventricular system, percutaneous cardiopulmonary support and for extracorporeal membrane oxygenation.
Table 3. Comparison of characteristics of roller and centrifugal pumps for cardiopulmonary bypass

|                          | Roller pumps                                                                 | Centrifugal pumps                                                  |
|--------------------------|------------------------------------------------------------------------------|-------------------------------------------------------------------|
| **Advantages**           | For repeated use; relatively cheap supplies                                 | The lack of probability of perfusion lines failure from excessive pressure in the system |
|                          | Simple sterilization                                                         | Decreased blood trauma                                             |
|                          | Easy to calculate perfusion speed (rotations per minute × stroke volume)     | Smaller risk of massive air embolism                              |
|                          | Variability of stroke volume depending on patients metrics                   | Lowe cavitation                                                   |
|                          |                                                                               | No wear of the lines                                               |
| **Disadvantages**        | Blood trauma                                                                 | Possibility of violation of the integrity of the closed perfusion circuit and stopping the pump due to excess pressure in the lines |
|                          | Possibility of violation of the integrity of the closed perfusion circuit and stopping the pump due to excess pressure in the lines | Different techniques to start the pump depending on the operator |
|                          | Retrograde blood flow during deceleration or stop of the pump                | More expensive pump with more expensive supplies                   |
|                          | Solid microemboli, cleaved from the lines into the circulating fluid          |                                                                   |
|                          | Possibility of massive air embolism                                          |                                                                   |
|                          | Variability of the occlusion degree influencing on the flow rate and degree of blood injury |                                                                   |
|                          | Contraindicated for long-term use due to the wear of lines and blood trauma  |                                                                   |

Advantages and disadvantages of roller and centrifugal pumps are listed in Table 3.

Centrifugal pumps are becoming more popular than roller pumps mainly due to the fact that they cannot create excessive pressure in the circuit and they are more preferable for use in terms of decreased blood trauma\(^1\). In our study it was shown that original centrifugal pump does not cause significant changes in different parameters of donor blood after 4 hours of perfusion, except for a moderate increase in free hemoglobin which does not exceed the same value for peristaltic pumps. It was also demonstrated that the studied pump incorporated into the apparatus for machine perfusion provides pressure-flow characteristics optimal for perfusion of the donor liver.

5. Conclusions

The experimental studies were performed with the original centrifugal pump that was developed as a part of the apparatus for machine perfusion of the donor liver. It was shown that after 4 hours of donor blood circulation in the closed circuit by means of the studied pump there were no significant changes in blood parameters except for increase in free hemoglobin concentration which was comparable to what happens during the perfusion with a roller pump. The centrifugal pump provides pressure-flow characteristics required for perfusion of donor liver both in arterial and venous lines. It can be noted that in cases of long-term cardiopulmonary bypass or mechanical circulatory support (particularly while maintaining the viability of the donor organ) centrifugal pump is superior to roller pump.

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7. References

1. McAnulty JF. Hypothermic organ preservation by static storage methods: Current status and a view to the future. Cryobiology. 2010; 60(3):13-19. Crossref PMid:19538951

2. Hashimoto K, Miller C. The use of marginal grafts in liver transplantation. Journal of Hepato biliary Pancreatic Science. 2008; 15(2):92-101.

3. Mulholland JW, Shelton JC, Luo XY. Blood flow and damage by the roller pumps during cardiopulmonary bypass. Journal of Fluids and Structures. 2005; 20(1):129-140. Crossref

4. Lopota AV, Gryaznov NA, Velichko OV. Technical Support of Preclinical Hydrodynamic and Functional Tests of New Medical Mechatronic Peristaltic Blood Pumps Developed by Central Research Institute of Robotics and Cybernetics. American Journal of Applied Sciences. 2016; 13(2):184-88. Crossref

5. Hessel EA. Cardiopulmonary bypass circuitry and cannulation techniques. Baltimore: Williams and Wilkins: Gravlee GP, Davis RF, Utley JR, (Eds.) Cardiopulmonary bypass, principles and practice. 1993; p. 55-92.

6. Kurusz M, Shaffer CW, Christman EW, Tyers GF. Runaway pump head: new cause of gas embolism during cardiopulmonary bypass. The Journal of Thoracic and Cardiovascular Surgery. 1979 May; 77(5):792-95. PMid:431117

7. Lynch MF, Peterson D, Baker V. Centrifugal blood pumping for open-heart surgery. Minnesota Medicine. 1978; 61(9):536-7. PMid:703742

8. Curtis JJ. Centrifugal mechanical assist for postcardiomyotomy ventricular failure. Seminars in Thoracic and Cardiovascular Surgery. 1994; 6(3):140-6. PMid:7948289

9. Nishida H, Shibuya M, Kitamura M. Percutaneous cardiopulmonary support as the second generation of venoarterial bypass: current status and future direction. Artificial Organs. 1993; 17(11):906-13. Crossref PMid:8110058

10. Black MD, Coles JG, Williams WG et al. Determinants of success in pediatric cardiac patients undergoing extracorporeal membrane oxygenation. The Annals of Thoracic Surgery. 1995; 60(1):133-8. Crossref

11. Kolff J, McClurken JB, Alpern JB. Beware centrifugal pumps: not a one-way street, but a dangerous siphon! The Annals of Thoracic Surgery. 1990; 50(3):512. Crossref