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Assessment of the Efficiency of a Single-Use Blood Pump in Hemolysis Tests

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The efficiency of a newly developed single-use blood pump was evaluated in comparison with the Safira single-use blood pump manufactured by Braile Biomedica (Brazil) used in modern clinical practice. The performance of prototype pumps was compared by evaluating the normalized index of hemolysis (NIH) calculated from data obtained during hemolysis tests. These studies showed that the level of hemolysis during perfusion using prototypes at this stage of development was not statistically different from that of single-use pumps used in clinical practice.

Introduction

The use of cardiopulmonary bypass (CBP) in cardiac surgery has become widespread in world clinical practice. Extracorporeal perfusion continues to be fundamental to cardiovascular surgery. In Russian clinical practice, cardiopulmonary bypass also occupies a significant place: 52,446 operations were performed using CBP in Russia in 2018 [1].

For Russian clinics, a complicating factor in the widespread use of this method is the lack of Russian-made cardiopulmonary bypass systems on the market. The development of a Russian centrifugal pump for use as part of a cardiopulmonary bypass circuit with characteristics close to imported analogs will reduce dependence on foreign manufacturers and expand the potential of using cardiopulmonary bypass in Russian clinical practice.

The use of CBP methods is associated with certain risks of developing complications. A significant proportion of this risk consists of systemic reactions by the body to the set of actions accompanying cardiac surgery [2]. Some adverse factors can be minimized at the level of the CBP apparatus, providing reductions in the loading on the body and increasing the efficiency of therapeutic actions. One of these factors is mechanical hemolysis of blood. The term hemolysis defines the destruction of red blood cells with release of free hemoglobin. The main criterion for successful operation of blood pumps used in cardiopulmonary bypass circuits, in addition to maintaining the required pressure and flow rate, is a minimal level of hemolysis.

It has been suggested that hemolysis caused by the use of CBP devices has a mechanical origin, i.e., is associated both with the hydrodynamic features of the blood flow through the system of artificial channels and with the properties of the channel walls: the intensity of the mechanical effect on the blood cells and the contact of cells with the surfaces of artificial vessels [3].

The aims of the present work were to carry out hemolysis tests on a prototype single-use blood pump (PT SUBP) developed at the Central Science Research and Experimental Design Institute of Robot Technology and Technical Cybernetics (CSI RTC) and to compare study parameters with those of a well-known analog, the Safira single-use blood pump (Braile Biomedica, Brazil).

This was addressed in terms of the following tasks:

1) development of a hemolysis test protocol for a single-use blood pump using donated blood;

2) identification and evaluation of the hemolytic characteristics of the pump under test for comparison with the characteristics of the reference pump.

The significant level of variation in the properties of blood taken from different donors makes it difficult in practice to normalize the extent of damage to blood cells. Parameters of different pumps were evaluated under sim-

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ilar experimental conditions in order to obtain objective results from comparison of the hemolytic characteristics of the pump under test and those of the Safira reference pump.

Materials and Methods

Blood coagulation, thrombus formation, embolism, and trauma to blood cells are to a large extent interrelated. Their main mechanisms are chemical and mechanical, but, in reality, neither one nor the other occurs separately [4, 5]. The clinical use of cardiopulmonary bypass devices causes metabolic shifts, which themselves can cause increased trauma to blood and intravascular coagulation and can increase mechanical and other actions on the blood passing through the device [6].

A number of tests were run to determine the intensity of the influences of the single-use blood pump (SUBP) design on blood cells during their passage through artificial vessels. The general view of the SUBP is shown in Fig. 1. The study was run using donated blood. Experiments did not use animal blood, as the formed elements of this material have significantly lower susceptibility to mechanical injury [7]. The selection criteria for the biomaterial included the donor having a normal body temperature at collection, the absence of signs of disease, and hematological parameters in the normal range. Blood with high lipid levels was excluded. The normalized index of hemolysis was selected as evaluation parameter for the action of SUBP on blood. The acceptable normalized index of hemolysis during a successful experiment should be no more than 0.04 g/100 L [8].

A commercial Safira centrifugal pump was used as a comparison (reference) pump. The characteristics of this pump were known in advance from the information materials published by Braile Biomedica [9].

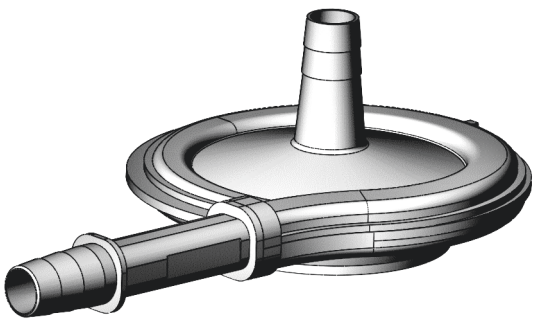

Fig. 1. General view of the single-use blood pump developed here.

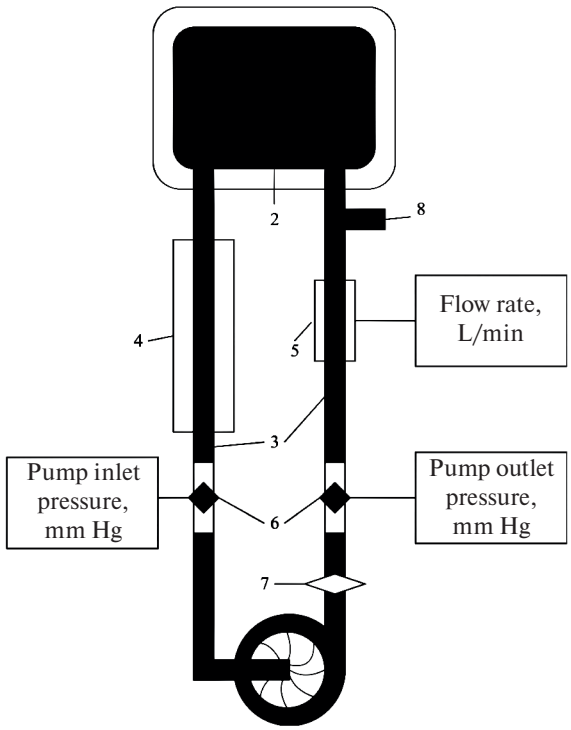

Fig. 2. Arrangement for hemolysis tests: 1) SUBP; 2) single-use blood tank; 3) blood lines; 4) heater; 5) flow sensor; 6) pressure sensors; 7) clamp; 8) blood sampling port.

Bench hemolysis tests for both PT SUBP and Safira pumps used the same pump drives (manufactured by the CSI RTC), and these were also positioned in the same way (horizontal arrangement of drives and pumps), standardizing the study protocol and excluding additional influences of the properties and operation of the pump drive on blood flow and particularly the state of erythrocytes. Figure 2 shows a diagram of the arrangement for hemolysis tests.

The test arrangement was a closed circuit, which included the single-use pump (SUBP) under study *1*, rigid blood tank *2*, flow meter *5*, heater *4*, two lines (PVC tubes) *3*, pressure sensors *6*, blood sampling valve *8*, and circuit pressure adjustment clamp *7*.

The following equipment was used to for measurement of flow parameters and analysis of blood:

1) an iStat hematology analyzer (Abbott, USA), for quantitative assessment of hemoglobin and hematocrit;

2) a RAPIDPoint 500 hematology analyzer (Siemens, Germany) for quantitative assessment of hemoglobin, hematocrit, and blood gases;

3) a HemoCue Plasma/LowHb low-hemoglobin analyzer (HemoCue AB, Sweden) with a measurement range

of 0-3000 mg% (mg/dL) and linearity over the range 30-3000 mg% (mg/dL);

4) a centrifuge for preparing plasma samples;

5) Combitrans pressure sensors (B. Braun, Germany).

Study parameters were recorded for 6 h for each sample of the single-use pump under study. The following operating parameters were maintained for all single-use blood pumps throughout the study: pressure drop $\Delta P >$ 250 mm Hg; flow rate $Q = 5 \pm 0.5$ L/min at supply voltage $U_{supply} = 2$ V, supply current $I = 0.35 \pm 0.03$ A. The pumps operated for 6 h and blood samples were taken every 30 min.

The intensity of blood hemolysis depends on many factors, which include both the quality of the blood itself and the hydrodynamic characteristics of the artificial blood line. A significant role related to the line is played by the smoothness of the surface contacting blood cells. Surface roughness in the blood line produces large increases in the calculated values of the shear stress acting on the erythrocyte membrane [10].

It should be noted that the first batch of PT SUBP (manufactured by CSI RTC) (No. 1-3) had assembly defects in the form of gluing defects. These defects increased surface smoothness. The relationship between the mechanical characteristics of the surface providing reductions in the intensity of mechanical action on blood cells and options for assembly providing the required product strength over the range of operating pressures needs to be considered. Samples No. 5-7 were resubmitted for testing.

Results

The results obtained here are presented in Table 1. This shows the initial conditions of the study (circuit filling volume, initial blood hemoglobin content (Hb), initial hematocrit (Hct), and free hemoglobin content at the beginning of the experiment), as well as results from measurements of free hemoglobin in blood throughout the perfusion time. The final change in the free hemoglobin level was assessed by calculating ΔfreeHb, which reflects the difference between the initial and final free hemoglobin levels in blood for each of the single-use pumps studied.

Table 1 shows that despite standardization of the study protocol, the initial blood indicators showed significant variation, due to the individual characteristics of the donor blood used.

Starting blood indicators were:

– for the PT SUBP (CSI RTC): Hct = 36 ± 5.6% and Hb = 122.3 ± 19.2 g/L;

TABLE 1. Overall Data from Hemolysis Tests

Time, min	Indicator/single-use pump No.	PT SUBP (TSNII RTK)			SUBP Safira (Braile Biomedica, Brazil)		
		No. 7	No. 6	No. 5	No. 1	No. 2	No. 3
–	Filing volume, mL	1049	1209	1602	1069	1069	1073
–	Hb, g/L	105	143	119	102	160	114
–	Hct, %	31	42	35	30	47	34
0	$freeHb_0$, mg/dL	1.5	2.6	2.5	2.5	2.3	2.3
30	$freeHb_{30}$, mg/dL	2.8	5.6	2.8	3.2	2.5	3.3
60	$freeHb_{60}$, mg/dL	3.8	8.1	3.4	4.5	2.3	4.7
90	$freeHb_{90}$, mg/dL	4.4	9.9	4.0	4.3	2.5	5.1
120	$freeHb_{120}$, mg/dL	5.4	11.7	4.7	5.3	2.5	5.3
150	$freeHb_{150}$, mg/dL	6.9	13.4	5.5	6.8	2.8	6.9
180	$freeHb_{180}$, mg/dL	8.2	15.1	6.3	8.2	2.6	8.7
210	$freeHb_{210}$, mg/dL	9.5	13.2	7.0	9.6	2.9	9.9
240	$freeHb_{240}$, mg/dL	10.7	14.0	7.8	10.9	3.0	11.0
270	$freeHb_{270}$, mg/dL	11.7	14.7	8.3	12.3	3.0	12.4
300	$freeHb_{300}$, mg/dL	12.9	15.6	8.8	13.8	3.2	12.5
330	$freeHb_{330}$, mg/dL	14.0	16.3	9.6	15.1	3.3	12.6
360	$freeHb_{360}$, mg/dL	15.1	16.8	10.1	16.3	3.4	12.9
–	ΔfreeHb	13.6	14.2	7.6	13.8	1.1	10.6

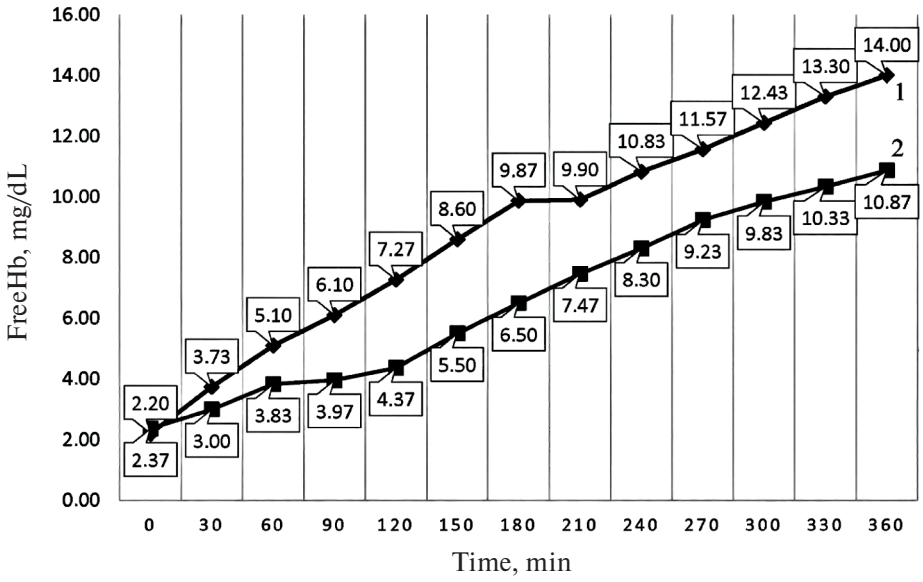

Fig. 3. Changes in the free hemoglobin content in blood over 6 h of perfusion: 1) SUBP (CSI RTC); 2) SUBP Safira (Braile Biomedica, Brazil).

– for the Safira SUBP (Braile Biomedica, Brazil): Hct = 37 ± 8.9% and Hb = 125.3 ± 30.6 g/L.

Figure 3 shows plots of changes in free hemoglobin contents (mean values) in blood throughout the entire perfusion procedure for the single-use pumps manufactured by the CSI RTC and Braile Biomedica respectively.

It follows from Fig. 3 that use of the SUBP produced by the CSI RTC gave higher blood free hemoglobin contents than in the Safira SUBP. However, Table 1 shows that ΔfreeHb calculated for the SUBP CSI RTC had a smaller spread than ΔfreeHb calculated for the Safira pump. Standard deviation $\Delta\text{freeHb}_{\text{SUBP CSI RTC}} = 3.65$ mg/dL, compared with $\Delta\text{freeHb}_{\text{Safira}} = 6.61$ mg/dL.

Numerical evaluation of hemolysis was obtained by calculating the normalized index of hemolysis (NIH) using the initial parameters of donor blood. NIH reflects the amount of free plasma hemoglobin released when a certain volume of blood passes through the extracorporeal circuit:

$$\text{NIH}\frac{g}{100l} = \Delta\text{freeHb} \cdot V \cdot \frac{100 - \text{Hct}}{100} \cdot \frac{100}{Q \cdot T},$$

where ΔfreeHb is the change in plasma free hemoglobin over the sampling period, g/L; V is the volume of the circuit, L; Q is blood flow, L/min; Hct is the hematocrit, %; and T is pump operation time, min.

The calculations showed that for the PT SUBP (CSI RTC), $NIH_{\text{CSI RTC}} = 0.0515 \pm 0.006$, and for the Safira pump, $NIH_{\text{SF}} = 0.034 \pm 0.028$ ($p > 0.05$).

Conclusions

Due to the small sample size, the value of 0.0515 for the PT SUBP (CSI RTC) should be regarded as acceptable in terms of statistical error in relation to the acceptable value for hemolysis of 0.04.

Taking into account the presence of gluing defects in the first batch of SUBP produced by the CSI RTC, which probably increased the smoothness of the internal surfaces, including gluing sites, we advise review of the techniques involved in polishing the internal surfaces and gluing the head as part of the mass production process and checking of the hermetic sealing of the assembly under pressure before release.

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