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BLOOD-RESERVING TECHNOLOGY IN SURGICAL CORRECTION

OF MITRAL VALVE DISEASES[[1]](#footnote-1)

USING THE CARDIOPULMONARY BYPASS

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This paper represents the results concerning 317 patients treatment with mitral valve deformities having been operated in the Department of Acquired Heart Diseases of the N.M.Amosov National Institute of Cardiovascular Surgery, the cardiopulmonary bypass having been used in all cases. All the patients observed were divided into two groups. The main group included 227 patients with mitral valve deformities; no donor blood preparations as well as blood-concentration columns or cell-savers were used for these persons’ treatment during their stay in the hospital. Several various blood-reserving approaches were elaborated and carried out in the Department during last 15 years[[4]](#footnote-4).

**Key words:** *cardiopulmonary bypass,* *blood-reserving technology, surgical treatment of mitral valve deformities.*

In essence, the transfusion of donor blood components is a variant of foreign tissue transplantation; it is accompanied by risks of different post-transfusional reactions and complications of both immune and non-immune origin. There is also a danger of various blood-borne infections[[5]](#footnote-5) (different hepatitides, AIDS, cytomegalovirus, syphilis, transfusion-caused mononucleosis, malaria etc.), their quantity becoming continuously higher. A proven fact is a marked immunosuppressional effect on the recipient’s organism following allohemotransfusions [1, 5-7, 10]. Currently, the clinicians become more and more often witnesses of ethical and juridical collisions due to patients’ refusal from allohemotransfusions because of doubtful donor blood safety as well as because of patients’ religious principles [10].

In should also mention a low functional efficacy of donor erythrocytic mass (EM) use because of sequestration of transfused erythrocytes (up to 25–30%) and decrease of their 2,3-diphosphoglycerate (2,3-DPG) content. In such conditions the hemoglobin-bound oxygen is poorly given to tissues. Thus, the transfused donor blood does not significantly improve the oxygen transport to tissues [1–7]. It is completely clear the problem of blood-reserving technologies to be an extremely burning one.

**The aim of this work** is to study up-to-date possibilities of blood-reserving[[6]](#footnote-6) approach in surgical correction of mitral valve deformities (MVD) using the cardiopulmonary bypass (CPB).

**Key words:** *cardiopulmonary bypass, approach without donor blood use, mitral valve correction.*

**Materials and methods.** During the period from the 01.01.2000 till the 01.01. 2016, workers of the Department of Acquired Heart Diseases of the N.M.Amosov National Institute of Cardiovascular Surgery were elaborating different approaches aiming to obtain blood-reserving technologies to be used in cases of surgical interventions necessary because of acquired valve pathology in conditions of cardiopulmonary bypass (CPB); in 937 cases the surgeons carried successfully out operations and the following patients’ hospital treatment without use of donor blood and its components. No hemoconcentrating columns or cell savers were also used.

This paper represents the results concerning 317 patients with MVDs treated in our Department and operated using the CPB from the01.01. 2004 till 01.01.2009. All the patients examined were divided into two groups; the main one included 227 patients with MDVs operated without introduction of donor blood preparations or of its components. Different variants of blood-reserving approaches were used for these patients’ treatment, no preparations of donor blood or its components having been introduced at any stage of the post-operative period.

The control group included 90 persons with the same pathology; however, no blood-reserving approaches were carried out; donor blood preparations or blood components were introduced both during intra-operative and post-operative period.

The main group contained 227 patients including 83 (36.6%) men and 144 (63.4%) women aged from 18 up to 70, their mean age being 51.3±9.6 yr. The control group consisted of 90 patients including 40 (44.4%) men and 50 (55.6%) women aged from 18 up to 70, their mean age being 47.6±9.3 yr. In all cases the MVD correction was made using the CPB.

Operations concerning isolated mitral valve prosthetics without any accompanying procedure are the most common ones; they were carried out in 138 (60.8%) patients of the main group as well as in 71 (78.9 %) patients of the control group.

During the treatment of the main group patients the authors have elaborated the approaches for blood-reserving technologies. Aiming to exclude any complication at any operation stage the authors carried continuously out a careful monitoring of all parameters – hemodynamics, acid-base balance (ABB) etc. Following three years of investigations (2000-2003) we have become able to understand completely the situation and to obtain methodological base for safe surgical interventions.

An important component of the main group treatment is the diuresis stimulation which started usually at the beginning of operation; the patients received furosemide (1 mg/kg) and mannitol[[7]](#footnote-7) (0.15–0.3 g/kg). The intravenous introduction of these drugs was carried out during 30 min in initial narcosis mixture. If the hematocrit value was above 0.4, it was possible to reserve the blood with citrate before the CPB beginning (A-variant of the blood reserving).

The higher is the initial hematocrit level, the larger blood volume can be reserved. The value of such autologous blood is due to its ability to keep all its properties during about 2 hours (time of the CPB duration), absence of heparin, and ability to rapid homeostasis restoration following protamine sulfate introduction. The autologous blood reservation according to the A-variant is a stage-by-stage patient’s blood collection into vials with a citrate preservative from the moment of incision up to the heparin introduction. The blood collection was mostly carried out through *arteria radialis* or sometimes through the central venous catheter during about 30 min under the strict arterial pressure (AP) control (Fig.1).

Thus, we were able to reserve the citrate blood (400 ml) for 104 patients (46%) before the CPB beginning, the blood volume was compensated by 10% refortan solution, the refortan:blood ratio being 1:1 (A-variant of blood reserving). The quantity of autologous blood reserved at the pre-infusion stage was 495.2±129.9 ml, i.e. 10.4±2.8% of the circulating blood volume (CBV). Following the autologous blood exfusion the hemoglobin level decreased from 134.5±14.6 g/l up to 130.4±16.8 g/l, the hematocrit index and the protein content fell down from 0.42±0.02 up to 0.39±0.05 and from 72.7±6.7 g/l up to 56.2±7.3 g/l, respectively; such decrease is safe: it does not significantly lower the blood oxygen capacity.

We have carried out comparative investigations of autologous blood state following its exfusion in the preservative glugycir (in the main group) and the state of donor EM used in the control group before it infusion to patients (see the Table 1).

Table 1

Acid-base equilibrium of autologous blood and donor erythrocytic mass

| Index | Autologous blood collected using the “Glugycir” (n=25) | Donor EM (n=21) | р value |
| --- | --- | --- | --- |
| Before re-infusion | Before re-infusion[[8]](#footnote-8) |
| pH | 6.84±0.1 | 6.89±0.08 | 0.052 |
| pCO2, mm Hg | 75.8±8.2 | 58.0±19.71 | 0.001 |
| pO2, mm Hg | 155.9±21.8 | 39.86±7.01 | <0.001 |
| BE[[9]](#footnote-9) | -20.7±3.4 | -22.53±2.54 | 0.774 |
| SO2, % | 96.2±1.9 | 45.0±4.6 | <0.001 |
| Storage time, min. | 230.6±54.8 | 5005.7±2755.6 | <0.001 |

The Table 1 data suggest the pH and **BE** indices for autologous blood and donor EM do not significantly differ. The indices of the blood oxygenation of the autologous blood collected using the “Glucygyr” from the *arteria radialis* are high enough (pO2 andSO2 valuesreach 155.9±21.8 mm Hg and 96.2±1.9 %, respectively), the oxygenation indices of the donor EM are not high (pO2 andSO2 valuesare 39.9±7.01mm Hg and 45.0±4.6 %, respectively) (р<0,001).

The duration of donor EM storage was rather short and did not exceed 3.7±0.7 days. In despite of identical changes of acid-base balance in autologous blood collected with the use of glugycir and in donor EM, the autologous blood transfusion is better for patients because of its better oxygenation indices, the minimal[[10]](#footnote-10) storage duration of such blood being 230.6±54.8 min. Besides, the own patient’s blood contains the complete set of clotting factors and active platelets [3, 7, 8].



Fig. 1. Depositing of autologous blood taken from the central vein before the beginning of perfusion. A-variant of blood reserving.

Following the aorta cannulation, the procedure of the retrograde autological priming (RAP) was realized in 46 patients (B-variant of blood reserving). It is possible in cases of stable hemodynamics when the patient’s body weight reaches 80 kg and more, the hematocrit value (according to the last analysis data) being not lower than 0.36. In these cases the heparinized blood is taken from the arterial line of CPB apparatus, the patient’s blood being collected into an oxygenator reservoir forcing out the initial bloodless perfusate which has been collected by a perfusologist in a separate reservoir (Fig. 2).



Fig. 2. Depositing of autologous blood in the CPB apparatus from the aortal main line before the perfusion beginning (RAP). The B-variant of blood reserving.

The task of this operation stage is to decrease as maximally as possible the hemodilution volume following the CPB beginning due to the CPB apparatus filling by the own patient’s blood. This procedure is usually carrying out under the strict hemodynamics control during about 9–10 min; thus, at this stage the use of any preparations lowering significantly the AP value (such as, for example, propofol) should be excluded.

During this period the operating surgeon carries out the vein cannulation and establishes a retrograde cannula. Using the B-variant of blood conserving (RAP) we have successfully forced out of the CPB apparatus reservoir 564.8±157.6 ml of the perfusate, i.e. 11.8±4.0% of the CBV.

If the blood analysis before CPB showed the hematocrit levels reaching 0.4 and higher, the patient’s weight being 80 kg or more and the oxygenator level being above 1500 ml, it was possible to realize the B-variant of blood reserving at the beginning of perfusion (Fig. 3).



Fig. 3. Perfusate deposition in the CPB apparatus from the venous main line during perfusion. The C-variant of the blood reserving.

We have successfully carried out this procedure in 34 cases as an isolated one and in 104 patients in combination with other variants (A or B). The exfusion volume of autologous blood perfusate passed through the venous oxygenator port was 495.8±148.8 ml (i.e.11.1±3.3% of the CBV), its calculated volume being 4.4±0.6 l).

After autologous blood exfusion on this stage the hemoglobin decrease was observed from 133.8±11.8 g/l up to 98.7±10.5 g/l, hematocrit and protein level having became lower from 0.40±0.04 up to 0.30±0.04 and from 71.8±6.0 up to 55.5±4.1 g/l, respectively; such situation is a safe one being not accompanied by significant drop of blood oxygen capacity.

Thus, the maximal autologous blood exfusion at operation stages for the variant «A+B+C» reached 1557.2±473.5 ml (i.e. 29.2±8.9% of the CBV), the minimal one being found for isolated A- (414.7±93.1 ml) and C-variants (495.8±144.8 ml) (see the Table. 2).

Table 2

Quantity of blood collected in different reservation groups

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Group of blood reserving | Blood exfusion, ml | RAP, ml | Blood exfusion at the beginning of perfusion from the CPB apparatus, ml | In all, ml | % from CBV |  |  |  |
| A | 495.2±129.9 |  |  | 495.2±129.9 | 10.4±2.8 |  |  |  |
| A+B | 414.7±93.1 | 555.8±129.8 |  | 970.5±222.9 | 22.5±4.7 |  |  |  |
| A+C | 447.2±91.2 |  | 501.9±159.9 | 949.1±251.1 | 19.1±5.1 |  |  |  |
| A+B+C | 490.5±144.6 | 573.8±185.5 | 492.9±143.4 | 1557.2±473.5 | 29.2±8.9 |  |  |  |
| C |  |  | 495.8±144.8 | 495.8±144.8 | 11.1±3.3 |  |  |  |

The variants of autologous blood reservation used in our work in the main group of patients are demonstrated in the Table 3.

Table 3

Variants of autologous blood reserving

| Group of blood reserving | Quantity of patients: |
| --- | --- |
| n | % |
| A-variant | 104 | 46.0 |
| A+B-variant  | 17 | 7.5 |
| A+C-variant | 53 | 23.3 |
| A+B+C-variant | 21 | 9.2 |
| C-variant | 24 | 11.0 |
| B-variant | 5 | 2.0 |
| B+C-variant | 3 | 1.0 |
| In all: | 227 | 100.0 |

According to the data presented in the Table 3, the most often used exfusion approach carried out both separately (in 104 patients, 46.0 %) and in combination with other exfusion methods (in 195 patients, 86.0 %) was the A-variant. The B-variant was used separately in 24 cases (11.0 %). Separated use of B- and B+C-variants of blood reservation was rare.

All the operations were carried out using the CPB and moderate hypothermic conditions (32–35 ºС). The myocardium protection was realized using a modified crystalloid St. Thomas solution supplemented with autologous blood (22.0%). The cardioplegia was usually carried out by retrograde introduction of cardioplegia-causing solution in combination with external heart cooling.

During the CPB, the following parameters were monitored: anticoagulation, gas blood content (GBC), ABB (РаО2: 100-300 mm Hg), SО2 (level of oxygen blood saturation), hematocrit, electrolyte level in the blood plasma, blood glucose, lactate, hemoglobin, and protein content, depth of anesthesia, diuresis (200 ml/h) during the hemodilution, temperature, central venous pressure (CVP) (negative), arterial pressure (APmean) (50-90 mm Hg).

After completing of the MVD correction and CPB arrest, the remainder from the reservoir was returned to the patient; the CBV was filled up under the strict hemodynamics control to avoid the heart over-loading. As a rule, isoket (0.5 μg/kg/min) was used at this stage to compensate maximally the perfusate for the patient from the oxygenator through the arterial main line. If it was not possible to realize such a procedure, the rest of the perfusate from oxygenator was collected into vials and injected to the patient intravenously. Thus, the irrevocable blood loss on this stage (the perfusate remainder in the reservoir) was minimized up to 20–25 ml. The careful surgical homeostasis was maintained at any operation stage.

 The CPB duration was 86,2±25,4 min, the time of the aorta clamping being 59.0±17.4 min in the main group; the same indices in the control group were 96.±14.2 min and 15.2 min, respectively (p>0,05).

One of the main principles of the CPB use is the absence of visible hemodilution at any correction stage. It permits to maintain the water equilibrium in terms of liquid before the perfusion beginning in the limits 0+300.0 due only to the 6 % refortan transfusion (about 400 ml as a compensation for the preoperative blood collection) and reaching almost zero water equilibrium level in the end of operation. It is especially important to minimize the water pre-loading on the pre-perfusion stage. In the overwhelming majority of cases this aim was reached using the refortan solution (6%, 400 ml).

On the CPB stage and in the end of perfusion the water equilibrium in terms of liquid did not exceed +1500.0 ml; in the end of operation this equilibrium reached as a rule the zero level due to the active diuresis. The calculated quantity of the protamine sulfate was introduced. Aiming the homeostasis improving, the gordox was injected in the end of operation (20.000–30.000 U/kg) as well as ε-aminocaproic acid (200 mg/kg) and etamsylate (30 mg/kg).

**Results and discussion.** No patient died in the hospital in both groups studied. The absence of allohemotransfusions in the main group patients promoted the decrease of post-operative complication quantity from 9.9% up to 2.2% comparing to the control group; the duration of artificial lung ventilation decreased from 12.3±11.5 hours up to 5.4±3.8 hours, the duration of intensive therapy having become shortened from 116.3±45.2 hours up to 56.4±22.7 hours (р<0,05). Thus, the blood reserving approaches in the main group proposed here permit to improve the results of surgical interventions aiming to correct MVDs.

The decrease of intra-operative blood loss belongs to the main tasks of operations being carried out without donor blood use. Having analyzed comparatively the volumes of intra-operation blood loss we have seen the loss in the main group of patients to be considerably lower than in the control one – 271.2±73.8 ml and 533.1±131.6 ml, respectively (р<0,05). The data concerning the blood loss volumes are shown in the Table 4.

Table 4

Intra-operative blood loss in cardio-surgical patients

and blood exudation through drainages in the ICU

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Main group (n=227) | % from CBV ОЦК | Control group (n=90) | % from CBV |
| Intra-operative blood loss, ml | 185.5±34.4 | 4.0±0.7 | 421.1±83.5 | 8.9±1.8 |
| Exudation through drainages, ml | 85.7±39.4 | 1.8±0.8 | 112.0±48.1 | 2.3±1.0 |
| In all, ml | 271.2±73.8 | 5.8±1.5 | 533.1±131.6  | 11.2±2.8 |

In the control group both donor blood and plasma were used at all operation stages in 90 patients (100%); in the intensive care unit (ICU) this approach included 48 patients (53.3%). In all, the EM volume transfused in the operation room to control patients reached 24.052 ml (i.e. 267.2 per patient), the freshly-frozen plasma volume being 30.585 ml, i.e. 340 ml per patient. In this group 32.317 ml of the EM were used, i.e. 359 ml per patient, and 44.510 ml of freshly frozen plasma, i.e. 495 ml per.

An important criterion of the blood oxygen capacity is the hemoglobin level at each correction stage. The dynamics of hemoglobin levels both in the main and in the control groups at all stages is given in the Table 5.

*Table 5*

Dynamics of Hb levels (g/l) in groups with blood reserving and in the control group at all operation stages

|  |  |
| --- | --- |
| Groups | Stages  |
| Beginningof narcosis | Beginning of operation  | Beginningof the CPB  | Endingof the CPB | Ending of the operation | 2nd day post operation | Discharge |
| A-variant(n=104) | 135.5±16.0 | 130.5±16.8 | 96.2±16.0 | 90.2±13.7 | 108.3±14.4 | 115.±18.9 | 110.9±13.0 |
| A+B-variant(n=17) | 131.2±15.3 | 128.7±16.6 | 99.5±11.2 | 95.1±12.2 | 115.4±9.7 | 128,4±16,9 | 107.0±18.0 |
| A+C-variant(n=53) | 139.9±16.1 | 132.2±14.8 | 99.5±11.9 | 95.1±11.8 | 109,5±11.9 | 127,2±16,0 | 110.8±13.1 |
| A+B+C-variant (n=21) | 140.4±12.1 | 131.3±15.9 | 103.1±14.6 | 96.1±9.2 | 116.3±9,8 | 131,5±18,6 | 120.0±10.9 |
| C-variant (n=24) | 133.8±11,8 | 133.9±17.6 | 98.7±10.5 | 93.4±10.4 | 110.4±8.1 | 124,6±19,5 | 109.1±11.1 |
| Control group (n=90) | 136,0±15,7 | 130.1±11.7 | 90.1±12.5 | 87.2±11.4 | 102.9±12.0 | 111,1±9,8 | 111.8±14.7 |

The Table 5 shows the hemoglobin levels to be adequate at each correction stage; it guarantees the safe level of the blood oxygen capacity confirmed by the absence of polyorganic insufficiency and clinically important complications during the hospital stage.

**Conclusions.** The method of surgical interventions without donor blood transfusions described above was introduced into the routine clinical practice for the MVD correction in the CPB conditions; thus, we obtained a good clinical efficacy without any transfusion-caused complications at the hospital stage [8-14]. The probability of this approach use lowers in patients whose weight is below 60 kg as well as in patients with anemia, with hemoglobin levels 110 g/l and below, and in patients aged above 65. The method of surgical interventions without donor blood transfusions should be used with precautions in cases of polyorganic insufficiency as well as in cases of initial considerable brain damage following the early happened disturbance of the brain circulation.

Indication criteria for intra-operative autologous blood reserving in cases of surgical MVD correction using the CPB are the following:

a) anamnesis data – absence in the case history of any information concerning anemia and withdrawal of drugs influencing on the blood clotting 7 days before operation;

b) initial laboratory indices concerning hemoglobin (≥ 120 g/l), hematocrit (≥ 40), platelets (≥ 170×109/l), erythrocytes (≥ 4,0×1012/l), and protein (≥ 60 g/l);

в) hemodynamics data following the initial narcosis when the CVP is ≥ 4 mm Hg and AP ≥ 90 Hg, the initial CBV being ≥ 4.4±0.7 l.

The variants of intra-operative autologous blood reserving being used for corrective MVD operations in CPB conditions and in combination with other approaches showed their efficacy; it permits to carry out such operations without use of donor blood and its components. The best results were obtained for the reserving variant A+B+C with the exfusion of the largest autologous blood volume – 1557.2±473.5 ml (i.e. 29.2±8.9% of the CBV); the statistically significant increase of platelets quantity (by 20.4%) was shown at the moment of patients’ discharge comparing to their initial data (р<0,05).

During operations of MVD correction in the CPB conditions the blood exfusion whose volume did not exceed 10-29% of the CBV caused no decrease of the oxygen delivery and oxygen consumption as well as no metabolic acidosis or lactoacidosis was found. In these cases the hemodynamics parameters were stable.

The ABB of the autologous blood collected into the glugycir is better comparing to the EM ABB. Primary damages occur in the autologous blood being exfused as a result of blood exit from its vascular bed and non-physiological storage conditions in the sodium citrate-containing medium; such damages have also place in the EM; they differ markedly from the physiological norm. The perfusate being reserved following heparinization in a vial without citrate-containing anticoagulant is kept in the conditions being “more physiological” ones.

The absence of allohemotransfusions in patients of the main group promoted the decrease of post-operational infectious complication quantity from с 7.7 % up to 2.2 % comparing to the control group.

The duration of the artificial lung ventilation[[11]](#footnote-11) and the duration of stay in the ICU for the main group decreased from 12.3±11.5 up to 5.4±3.8 hours р<0.05) and from 116.3±45,2 up to 56,4±22,7 hours (р<0,05), respectively, comparing to the control group; thus, we obtained better results of surgical correction for MVD patients.

The authors improved also the current method of operation anesthetic support concerning: a) carrying out of infusion and transfusion therapy (stimulation of diuresis, water balance control, and acute normovolemic dynamics[[12]](#footnote-12) before the CPB and decrease of hemodilution due to the retrograde oxygenator filling by autologous blood; b) perfection of autologous blood exfusion methods and their combination, change of infusive hemostatic therapy approaches; c) CVP control and AP maintaining when realizing different autologous blood exfusion procedures. All these improvements have increased the quality of surgical interventions for MVD patients in CPB conditions.

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