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V.I. Cherniy, L.O. Sobanska, P.O. Topolov
State Institution of Science "Research and Practical Center of Preventive and Clinical Medicine" State Administrative Department, Kyiv

EFFECT OF PRIMING SOLUTIONS IMPROVEMENT ON METABOLISM ASSOCIATED WITH CARDIOPULMONARY BYPASS

e-mail: sobanskayalada@gmail.com

Improving metabolism by optimizing the composition of the priming during on-pump coronary artery bypass grafting was the aim of this study. The 30 patients were divided into two groups. In group 1, priming included succinated gelatin 4 %, mannitol 15 %, Soda buffer 4.2 %, Reosorbilact, heparin. In group 2, priming included succinated gelatin 4 %, mannitol 15 %, sodium bicarbonate 4 %, 0.9 % sodium chloride, heparin. It has been shown that cardiac patients have preoperative metabolic disorders. In group 1 the metabolic rate index was 425.61±27 kcal/min/m², and the target metabolic index was 576.79±16 kcal/min/m². In group 2, 355.98±32 kcal/min/m² and 689.28±21 kcal/min/m², respectively. In group 1, the metabolic rate index metabolism was differed from the target by 27 %, and in group 2 – by 52 %. One of the methods for improving perioperative metabolism is the optimization of the priming composition under the control of energy monitoring.

Key words: cardiac surgery, cardiopulmonary bypass, priming, perioperative energy monitoring, metabolism, coronary artery bypass grafting.

В.І. Черній, Л.О. Собанська, П.О. Тополов

ВДОСКОНАЛЕННЯ СКЛАДУ ПЕРВИННОГО ОБ'ЄМУ ЗАПОВНЕННЯ ОКСИГЕНАТОРА ДЛЯ ПОЛІПШЕННЯ МЕТАБОЛІЗМУ ПРИ ШТУЧНОМУ КРОВООБІГУ

Метою даного дослідження було поліпшення метаболізму за рахунок оптимізації первинного об'єму заповнення оксигенатора при аортокоронарному шунтуванні зі штучним кровообігом. 30 пацієнтів були поділені на дві групи. В групі 1 до перфузату входили розчин желатину сукцинільованого 4 %, маніт 15 %, Сода-буфер 4.2 %, Реосорбілакт, гепарин. В групі 2 використавували розчин желатину сукцинільованого 4 %, маніт 15 %, натрію гідрокарбонат 4 %, 0,9 % натрію хлорид, гепарин. В групі 1 показники індексу поточного метаболізму склали 425.61±27 kcal/min/m², а цільового 576.79±16 kcal/min/m². В групі 2 355.98±32 kcal/min/m² та 689.28±21 kcal/min/m² відповідно. В групі 1 поточний метаболізм відрізнявся від цільового на 27 %, а в групі 2 на 52 %. Одним зі способів поліпшення періопераційного поточного метаболізму є оптимізація складу первинного об'єму заповнення оксигенатора під контролем персоніфікованого енергомоніторингу.

Ключові слова: кардіохірургія, штучний кровообіг, первинний об'єм заповнення оксигенатора, періопераційний енергомоніторинг, метаболізм, аортокоронарне шунтування.

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Contemporary extracorporeal technologies have high efficiency. Despite the improvement of cardiopulmonary bypass (CPB), the metabolism continues to be underinvestigated. One of the ways of studying metabolism is indirect calorimetry, which is based on oxygen consumption, with consideration for oxygen energy equivalent. It has been proven that the level of perioperative energy production and its energy supply play an important role in the security of anaesthetic and surgical technologies [8].

It is known that the priming of the CPB circuit is one of the first potential factors that can lead to a negative effect on metabolism [14]. For that reason, finding a composition of priming volume is very important for patients who need cardiac surgery. Despite discussion on this scientific topic, there is not a consensus of opinions about the best composition priming volume of the CPB circuit. The generally accepted approach involves using two types of priming: crystalloids and colloids [11]. In practice, crystalloid priming volume usually includes only electrolyte solutions, but colloid priming volume is composed of human albumin (HA), dextran, gelatin, and hydroxyethyl starch (HES) [5, 10, 12, 15]. As a rule, both types of priming have additional additives such as mannitol and sodium bicarbonate.

Much research has been aimed at studying priming advantages and disadvantages in terms of effects on the clotting system, haemostasis, non-surgical bleeding, hemodilution, interstitial oedema, metabolic acidic state and colloid oncotic pressure [6].

In this study, we based on the take-home message that priming is one of the main factors to ensure an adequate metabolism. In order to do that, priming volume have to satisfy the conditions: ensuring moderate hemodilution, without excessive volemic loading; maintaining the balance of electrolytes and acid-base status; ensuring the avoidance of a decrease in colloid-oncotic pressure with the beginning of CPB; implementation of the positive effect of the total osmotic concentration solutions on the state of cells; minimizing trauma to blood cells; maintenance the sustainable functioning of the oxygen transport system blood functions.

The purpose of the study was to evaluate the possibility of using personalized energy monitoring during cardiopulmonary bypass and improving perioperative metabolism during perfusion due to the composition of the priming volume of the oxygenator circuit.

Materials and methods. The study included 30 patients who underwent on-pump coronary artery bypass grafting (CABG). The patients were divided into two groups. The first composition of the priming included a solution of succinylated gelatin 4 %, Mannitol 15 %, Soda-buffer 4.2 %, Reosorbilact and heparin (group 1, n=15) [3]. The second composition of the priming included 4 % succinylated gelatin, 15 % mannitol, 4 % sodium bicarbonate, 0.9 % sodium chloride and heparin (group 2, n=15). There was no statistically significant difference by gender, age, body surface area ($p>0.05$ for each parameter). Patients in two groups had functional class III by classification of The New York Heart Association functional classification (NYHA). The main stage of the operation was performed on ventricular fibrillation, without the use of cardioplegic solutions.

Duration of CPB than 120 minutes, donor blood used during perfusion and surgical complications in the early postoperative period that need urgent re-surgical intervention in the first 24 postoperative hours were withdrawal criteria from the study.

A membrane oxygenator, a roller pump (Stockert S5), nonpulsatile flow and moderate hypothermia (32±1°C) were used for perfusion. Cardiopulmonary bypass target data are blood flow rate (BFR) 2.5–3 l/min/m², mean arterial blood pressure (MAP) 60–80 mmHg, central venous pressure (CVP) 2–5 mmHg, urine output > 1 ml/kg/h and moderate hemodilution with haematocrit (Ht) 25±2 g/l.

The total volume of solutions used to fill the CPB circuit depended on the base hemoglobin and the hemoglobin level that we expected to gain during CPB. The formula for volume used in priming the CPB oxygenator and circuit:

$$\text{Priming (ml)} = \text{CBV (ml)} \times \text{Hbbase}/\text{Hbcpb} - \text{CBV (ml)} \quad (1)$$

where CBV – circulating blood volume of patient; Hbbase – base hemoglobin before CPB; Hbcpb – hemoglobin level that we expect to gain during CPB.

Rewarming of patients during CABG-3 began from the moment of formation of the last distal anastomosis with the native coronary artery. The average speed of rewarming was 1°C per 3–4 minutes. By the time the mammary coronary anastomosis with the left coronary artery was formed, the temperature of the patients was 35.3±1.5°C. The final rewarming of the patients was during the period of formation of the proximal anastomoses.

For intraoperative monitoring, we used laboratory (Hb, Ht, arterial and venous blood gases, acid-base balance), calculated (osmolarity of plasma and priming, estimated level of hemodilution) and instrumental (mean arterial pressure) research methods. Oxygen delivery (DO2), oxygen consumption (VO2), Oxygen Extraction Ratio (O2ER), Respiratory quotient (RQ) was used for the analysis of blood oxygen status. To calculate oxygen consumption, we used the parameter of mixed venous oxygen saturation (SvO2). BFR is an analogue of the cardiac index (CI) during CPB. Condello et al. [7] proposed a method, when CI was managed in relation to SvO2 (the cut off for increase in CI was<75 % SvO2, the cut off for decrease in CI was>75 % SvO2. Also, Condello et al. [7] indicated that SvO2, in the clinical and intensivist practice, was a true reflection of the global balance between oxygen delivery and consumption because it is measured through the venous drainage line during CPB where venous blood returning to the right heart from the superior vena cava, inferior vena cava, and the coronary sinus have mixed. SvO2 has been extensively studied and used clinically to monitor the global balance between DO2 and oxygen consumption.

To study metabolism, all patients underwent personalized energy monitoring at the stage of rewarming (when the body temperature reached 36.5–36.7˚ C). This technique is based on the use of indirect calorimetry. The Metabolic Rate Index (MRI, kcal/min/m²) and the Target Metabolic Rate Index (TMRI, kcal/min/m²) were determined. MRI and TMRI made it possible to judge the severity of metabolic disorders. This indicator is referred to as Index Metabolic Disorders (IMD, %) [9].

The obtained quantitative parameters are checked. Data of study are normally distributed. Data are presented as mean (M) and its standard error (SD) were determined. The Student's *t*-test is used to compare the means between two groups. A p-value of 0.05 as the limit of statistical significance was accepted. Statistical analysis was performed using the statistical software (licence certificate v. 4. MS 000070-06.07.2009, Y. Y. Liakh, V. G. Gurianov).

Results of the study and their discussion. Before cardiopulmonary bypass, there was no statistical difference in HB ($p=0.159$), Ht ($p=0.265$) and MAP ($p=0.395$) when the group1 and group 2 were compared.

Results of the study of oxygen status and metabolism before CPB are presented in Table 1.

Table 1

Precardiopulmonary bypass profile of oxygen status and metabolism

Parameters	Mean±SD		p
	Group 1 (n=15)	Group 2 (n=15)	
CI, l/min/m²	2.38±0.12	2.27±0.16	0.517
IDO2, ml/min/m²	375.46±28.17	369.98±29.31	0.281
IVO2, ml/min/m²	87.48±6.31	85.29±5.17	0.678
O2ER, %	23.29±1.72	23.17±1.98	0.911
RQ	0.80±0.03	0.81±0.01	0.243
MRI, kcal/min/m²	486.43±16	490,35±19	0.097
TMRI, kcal/min/м²	553.75±19	549.36±20	0.069
IMD, %	6.33±0.21	5.99±0.34	p=0.082

Notes: CI – cardiac index, IDO2 – oxygen delivery index, IVO2 – oxygen consumption index.

There was no statistical difference in both groups that indicates the same conditions for production and supply of energy. It corresponds to no statistical differences in the level of consumption and delivery of oxygen under normal values of the oxygen extraction ratio. It is significant that the initial metabolic values for both groups tended to be impaired in both group with no statistical difference in IMD. It shows that cardiac surgery patients are at risk for metabolic disorders.

The mean CPB-time was 74±15 min in group 1 and 79±11 min in group 2 (p=0.735). The total volume priming in group 1 was 1310±123 ml and in group 2 1450±115ml without statistical significance (p=0.653).

Determination of Hb at the rewarming stage showed that in group 1 there was a tendency (p=0.053) to higher Hb – 89.21±12.92 g/l) compared to group 2 – 83.14±14.65 g/l. Urine output was better in group 1 – 8.5 ml/kg/h than in group 2 – 6.7 ml/kg/h (p>0.05).

Parameters of oxygen status and metabolism in the studded groups during CPB at the rewarming stage are presented in Table 2.

Table 2

Oxygen status and metabolism during CPB at the rewarming stage (t=36.5±0.3°C)

Parameters	Mean±SD		p
	Group 1 (n=15)	Group 2 (n=15)	
BFR, l/min/m²	2.5±0.19	2.6±0.15	0.789
IDO2, ml/min/m²	341.21±79.13	289.27±68.19	>0.05
IVO2, ml/min/m²	84.32±24.91	72.98±31.25	>0.05
O2ER, %	24.77±0.94	24.82±1.03	0.952
RQ	0.87±0.02	0.83±0.03	0.05
MRI, kcal/min/m²	425.61±27	355.98±32	>0.05
TMRI, kcal/min/m²	576.79±16	689.28±21	>0.05
IMD, %	13.56±0.23	22.89±0.29	>0.05

To assess metabolism, it is important that the BFR in both groups is not statistically significant (p=0.789). The target metabolic rate is the desired permissible level that ensures a non-deficient oxygen status and a metabolic level that corresponds to the individual's optimal level of metabolism at a particular point in time. The metabolic rate is the metabolism that exists at a particular time in a patient. In our study, we correlated the MR and TMR with the body surface area. It was found that MRI and TMRI were statistically different in groups 1 and 2. MRI differed on average by 27 % and 52 % from TMRI in groups 1 and 2, respectively. As a result, in group 1 MRI was closer to TMRI than in group 2 (p>0.05). It indicates a greater bioenergy reserve in group 1.

It was determined that CPB causes metabolic disorders. At the stage of rewarming in group 1, the index of metabolic disorders was lower than in group 2 (p>0.05).

The data resulting from the study indicate the possibility of correcting metabolism by optimizing the composition of the priming. Blood oxygen saturation is determined according to the partial pressure of oxygen, the hydrogen ion concentration and bicarbonate (formula of the mathematical model of the Bohr effect). Usually, in practice, use a 4 % sodium bicarbonate solution with a pH of 7.4–8.5. The main disadvantage of this solution is the sharp shift in blood pH and the transition to a state of alkalosis, which can persist for a long time. It is difficult to correct and leads to severe complications. This effect is associated with an abrupt and unbalanced increase in the concentration of bicarbonate ions, which occurs with a relative deficiency of carbon dioxide. Also, the administration of overdoses of sodium bicarbonate is not effective in correcting pH. With excessive administration of soda, carbon dioxide is not completely

eliminated by the lungs, but diffuses into cells, where hydrogen ions are formed with the participation of water. It leads to intracellular alkalosis. This is known as alkalosis, oxygen uptake in the lungs is facilitated due to the Bohr effect, but its release to the tissues is complicated, directly affecting metabolism in the tissues [4, 13]. The solution of 4.2 % Soda buffer is buffered with carbon dioxide to a physiological pH = 7.3–7.4 and has a normal HCO3/CO2 ratio of 20/1, does not have such disadvantages, normalizing the affinity of blood for oxygen.

The ability to increase the alkaline reserve of the blood and its oxygenation, without significantly affecting the level of carbon dioxide tension in the blood, is one of the advantages of Reosorbilact. The solution composition serves as an energy substrate with a mild adrenomimetic effect due to the synergy of sorbitol and adrenaline. It leads to improved microcirculation and tissue metabolism. Sorbitol in the composition of Rheosorbilact helps to normalize carbohydrate and energy metabolism and has a powerful specific osmotic diuresis effect in conditions of hemodilution [1, 2]. It helps to increase decreased hemoglobin during CPB. It corresponds with our study, according to which diuresis and metabolism were statistically preferable in the group where Reosorbilact was used.

Conclusion

1. Cardiac surgery patients are at risk for metabolic disorders. It is the basis for the need to use perioperative energy monitoring

2. In the case of preoperative changes in metabolic homeostasis, it should be taken into account that surgery may further increase existing disturbances.

3. Cardiopulmonary bypass enhances already existing metabolic disorders in cardiac surgery patients.

4. The composition of the priming influences the metabolism during cardiopulmonary bypass. One of the methods for improving perioperative metabolism is the use of Soda-buffer 4.2 % and Reosorbilact as the priming components.

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