

# Disturbance of Acid-Base Balance in Surgical Treatment of Septic Endocarditis

Sh. A. Islambekova, L. A. Nazirova, Sh. M. Aliev

Republican Specialized Center of Surgery Named after Academician V. Vakhidov, Tashkent, Uzbekistan

**Abstract** **Aim** of our study was to assess the acid-base state (ABS) in patients with septic endocarditis (SE) in perioperative period. **Material and methods.** The research has been based on the analysis of 108 patients with septic endocarditis. The main group included 24 patients who used zero balance ultrafiltration (Z-BUF) of blood during cardiopulmonary bypass (CPB). Control group included 84 patients who were not used Z-BUF. Cardiopulmonary bypass was performed on a "Sarns Terumo" apparatus. Blood analysis of the acid-base state in all groups was carried out on ABL-735 apparatus produced by "Radiometer" (Denmark). Statistical processing was carried out using the MS Excel applied software package, STATISTICA 10.0. To assess the normality of the sample distribution, the Kolmogorov-Smirnov tests for samples  $n > 50$  and Shapiro-Wilk tests for samples  $n < 50$  were used. Statistical hypotheses about the equality of general means were tested to identify the difference between the groups. Quantitative data have been presented as  $M \pm \sigma$ , logical data - as a share of the total number of observations.  $X^2$  test with Yates's correction and McNemar was used to compare qualitative features. Data were considered statistically significant at  $p < 0.05$ . **Results.** The results of our research showed that after induction of anesthesia, patients in the groups had fully compensated chronic respiratory alkalosis. Hypocapnia was more evident in Z-BUF group and significantly differed from the comparison group ( $p=0.01$ ). At the end of the cardiopulmonary bypass (CPB), the pH in the main group remained within the normal range, while in the comparison group, an increase in pH ( $p=0.005$ ) towards alkalosis was revealed. Anion gap of plasma was more than 12 mEq/L in the Z- BUF group: before CPB 7 (29%), after CPB 3 (12.5%); in the comparison group: before CPB 17 (20.2%) after CPB 7 (8.3%),  $p > 0.05$ . The proportion of patients with low anion gap did not increase after CPB in the Z-BUF group (before CPB (12.5%), after CPB (12.5%)), while in the comparison group, low anion gap increased from 4 (4.76%) to 22 (20.1%) cases. **Conclusion.** Z-BUF supports the compensatory mechanism of respiratory alkalosis in patients with septic endocarditis during cardiopulmonary bypass. Z-BUF reduces hemodilution and maintains a normal level of albumin in blood during cardiopulmonary bypass. Z-BUF reduces the level of potassium ions in blood by eliminating them during filtration, which is a necessary property during hyperkalemic cardioplegia.

**Keywords** Septic, Endocarditis, Cardiopulmonary bypass, Perioperative period, Blood ultrafiltration, Respiratory alkalosis, Acid-base state, Bicarbonates

## 1. Introduction

Currently, many aspects of the diagnostics and surgical treatment of septic endocarditis (SE) remain relevant. It is mainly connected with an increase of morbidity and a change in the clinical picture of this nosology. Patients are admitted to hospitals with advanced forms of endocarditis, with low myocardial reserves and with the development of life-threatening complications [1]. Kidney damage is often the first clinical manifestation of the disease and occurs from 2 to 78% [2]. Mortality among SE patients with kidney involvement is significantly higher than in patients without this complication [2]. Cardiac surgeons are faced with the question of the possibility and safety of surgical treatment in

the conditions of the kidney pathology. Cardiopulmonary bypass (CPB) which is a fundamental component of cardiac surgery, has its drawbacks. Contact of blood with the surface of the extracorporeal circuit, hemodilution, hypothermia trigger the release of numerous inflammatory mediators and imbalance of cytokines and other factors that lead to endothelial damage, contraction of endothelial cells and an increase of capillary permeability [3]. Massive release of fluid from the vascular bed into the intercellular space leads to disruption of tissue metabolism, hypoxia and organs' edema [3-4]. Improvement of surgical technique and optimization of cardiopulmonary bypass can reduce postoperative complications. The use of the method of blood ultra-filtration (UF) in the protocol of cardiopulmonary bypass is widely covered in the works of various authors [4-8]. Currently, the effectiveness of blood ultra-filtration and its effect on the function of vital organs and systems

(hemodynamics, contractile function of the heart, ventilation of the lungs, cerebral blood flow, postoperative blood loss) are widely studied, but there are also conflicting opinions about their capabilities [4-8]. Thus, a number of studies have shown the role of blood UF in the increase of metabolic acidosis due to the active elimination of bicarbonate buffer [9]. According to some authors view, the use of sodium bicarbonate solutions for the correction of metabolic acidosis leads to an increase of a large amount of carbonic acid and CO<sub>2</sub> in the blood plasma which requires an increase in the volume of pulmonary ventilation and worsens the condition of patients with respiratory failure [10]. Considering that not only the kidneys but also the lungs are damaged during SE, the correction of metabolic disorders at this pathology requires a special approach.

**Aim** of our study was to assess the acid-base state (ABS) in patients with septic endocarditis (SE) in perioperative period.

## 2. Material and Methods

The research has been based on the analysis of 108 patients with septic endocarditis: 63 (58%) males and 45 females (42%). The mean age of patients made up  $41.50 \pm 11.57$  years. The severity of the patients' condition with chronic heart failure (CHF) was evaluated in accordance with the classification of CHF of the New York Heart Association (NYHA, 1994). The main group included 24 patients who received balanced blood UF during cardiopulmonary bypass (CPB). The control group included 84 patients who did not receive blood UF. There were no significant differences between the groups in age, sex, body surface area and comorbidities. Indications for blood UF during CPB were: chronic kidney disease with a decrease in the glomerular filtration rate  $GFR < 60 \text{ ml / min / } 1.73 \text{ m}^2$ , signs of kidney damage (proteinuria, leukocyturia, hematuria), an increase in the left ventricular end-diastolic volume of more than 250 ml (large inflow into the venous reservoir of the oxygenator), CPB for a long time (more than 120 min), moderate anemia, concomitant diseases and cardiorenal syndrome when there is no possibility of using diuretics. The main group significantly differed by more severe clinical course before surgery: functional class (FC) IV was detected in 6 (25%) patients and FC III in 18 (75%) patients according to NYHA, in contrast to the control group, where FC IV was recorded in 6 (7.1%) patients and FC III in 78 (92.8%) patients according to NYHA at  $\chi^2=6,03$ ;  $p < 0,05$ .

Cardiopulmonary bypass was performed on a Sarns Terumo apparatus. Membrane oxygenators "Skipper-Euroset" (Italy) were used. Blood analysis of the acid-base state in all groups was carried out on ABL-735 apparatus produced by "Radiometer" (Denmark). The collection of the ABS analysis was carried out at the following stages of perfusion: before the start of CPB for 5 min of conducting CPB; after CPB; before taking the

patient out of the operating room; in the intensive care unit. The following indicators were examined in the obtained blood samples: hematological (Hb, Ht), physico-chemical (pH, BE, HCO<sub>3</sub><sup>-</sup>, osmolarity, pO<sub>2</sub>, pCO<sub>2</sub>, SatO<sub>2</sub> of arterial blood), biochemical (glucose, lactate), electrolyte composition (Na<sup>+</sup>, K<sup>+</sup>, Ca<sup>2+</sup>).

CPB was performed under moderate hypothermia (32°C). Blood pressure was maintained at a level not lower than  $72.9 \pm 6.88 \text{ mm Hg}$ . For ultrafiltration of blood, we used HPH 700 Medtronic hemoconcentrators (USA) with a pore diameter of 65000 Da. The removed ultrafiltrate was replaced with a balanced electrolyte Ringer-Locke solution or saline (0.9% sodium chloride) with the addition of 10% 10.0 calcium chloride and 8% 50.0 sodium bicarbonate (soda) per 1000 ml of infused liquid. The following parameters were assessed to characterize the acid-base state (ACS): blood buffer systems; carbonate level (HCO<sub>3</sub><sup>-</sup>), standard bicarbonates (SBC), buffer bases (BE), partial pressure of carbon dioxide (pCO<sub>2</sub>), oxygen partial pressure (pO<sub>2</sub>), alkaline blood reserve, ion concentration [H<sup>+</sup>], pH, lactic acid concentration. To evaluate metabolic acidosis, the plasma anion gap (PAG, mEq / L) and the differential coefficient were calculated using the formulas:  $PAG = [Na^+] - ([Cl^-] + [HCO_3^-])$  and  $PAG/[HCO_3^-]$ , respectively. Simple types of acid-base imbalance were diagnosed based on the analysis of three parameters determined in an arterial blood sample: pH, plasma bicarbonate concentration (HCO<sub>3</sub><sup>-</sup>) and pCO<sub>2</sub>.

Statistical processing was carried out on a personal computer - IBM Pentium with Windows 7 operating system using a package of applied software MS Excel, STATISTICA 10.0. For statistical analysis of the data, the following methods were used: parametric statistical methods (Kolmogorov-Smirnov test for samples  $n > 50$  and Shapiro-Wilk for samples  $n < 50$ ). Descriptive statistics was used to detect and analyze causal relationships between variables. Statistical hypotheses about the equality of Student's t-test general means were tested to identify the difference between the groups. To compare qualitative features, a chi-square was used with Fisher's test and with Yates' correction. Data were considered statistically significant at  $p < 0.05$ .

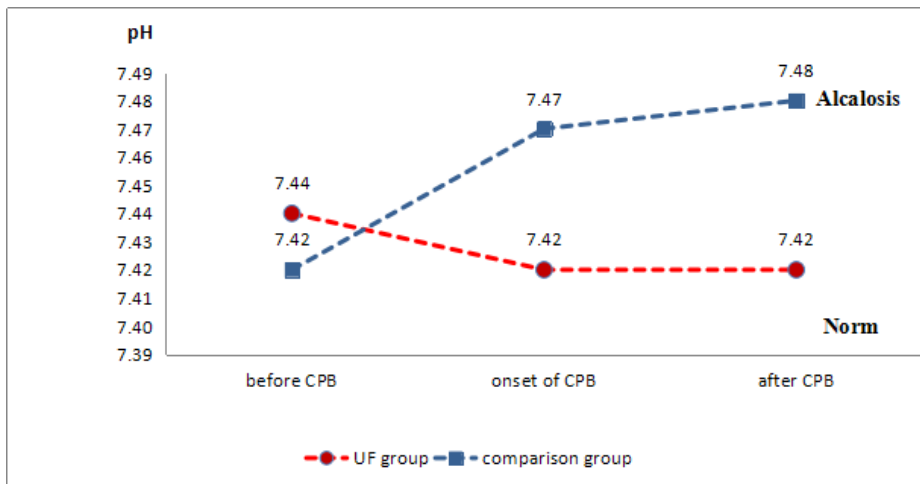
## 3. Results and Discussion

The groups did not differ in the duration of CPB (main group -  $87.2 \pm 28.1 \text{ min}$ , control group -  $80.0 \pm 25.3 \text{ min}$ ,  $p > 0.05$ ) and the time of aortic clamping (main group -  $66.3 \pm 24, 1 \text{ min}$ , control group -  $60.4 \pm 18.0 \text{ min}$ ,  $p > 0.05$ ). The minimum hemoglobin during CPB in the groups was significantly different (main group:  $80.0 \pm 13.4 \text{ g / L}$ ; comparison group  $88.7 \pm 11.7 \text{ g / L}$ ; at  $t = 2.80$ ;  $p = 0.009$ ). In the UF group, the level of minimum hemoglobin (Hb =  $80.0 \pm 13.4 \text{ g / l}$ ) was sufficient for adequate oxygen delivery to tissues of DO<sub>2</sub> and was maintained at a level above the "critical"  $330 \text{ ml / min-1 / m-2}$  ( $523.0 \pm 114, 7 \text{ ml / min-1 / m-2}$ ).

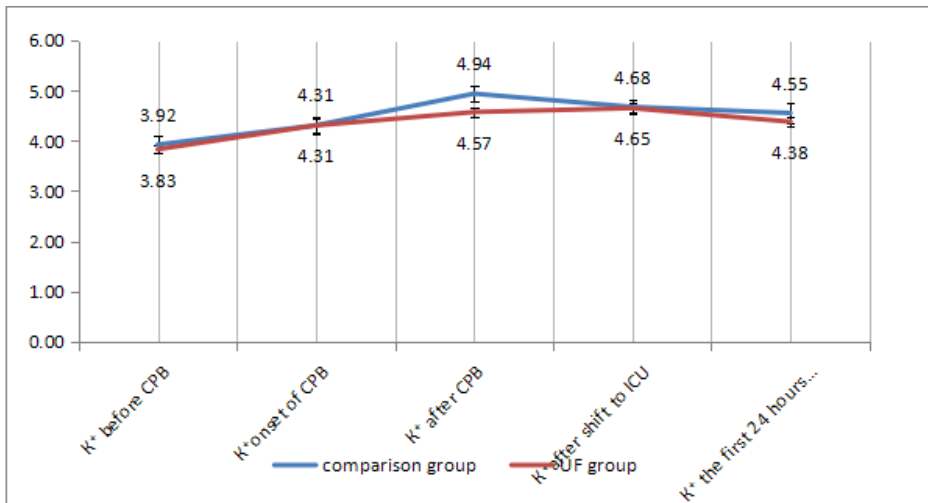
m-2.) at a CPB temperature of  $32.4 \pm 1.43^\circ\text{C}$ . After CPB, the hemoglobin and hematocrit values in the groups did not differ statistically ( $p = 0.77$ ) and the hemoglobin value was above  $90 \text{ g/l}$ .

**Table 1.** Indicators of acid-base balance in groups in the perioperative period

| Indices  |              | Main group<br>n=24 |      | Control group<br>n=84 |      | T<br>Critical<br>1.98 | p            |
|--|--------------|--------------------|------|-----------------------|------|-----------------------|--------------|
|  |              | M                  | s    | M                     | s    |                       |              |
| pH of blood                                      | before CPB   | 7.44               | 0.09 | 7.42                  | 0.05 | 0.75                  | 0.38         |
|  | onset of CPB | 7.42               | 0.11 | 7.47                  | 0.06 | 1.68                  | >0.05        |
|  | after CPB    | 7.42               | 0.07 | 7.48                  | 0.10 | <b>3.16</b>           | <b>0.005</b> |
| PaCO <sub>2</sub><br>mmHg                        | before CPB   | 31.1               | 5.38 | 34.3                  | 4.96 | <b>2.21</b>           | <b>0.01</b>  |
|  | onset of CPB | 30.8               | 6.73 | 27.6                  | 4.50 | 1.79                  | >0.05        |
|  | after CPB    | 31.7               | 7.0  | 29.4                  | 6.27 | 1.19                  | 0.17         |
| Supposed PaCO <sub>2</sub> ( $\pm 2$ ) after CPB |              | 40.7               | 3.21 | 41.6                  | 2.36 | 1.04                  | 0.22         |
| HCO <sub>3</sub> <sup>-</sup><br>mmol / l        | before CPB   | 20.6               | 3.48 | 21.6                  | 2.27 | 1.12                  | 0.19         |
|  | onset of CPB | 19.2               | 2.42 | 19.4                  | 1.81 | 0.27                  | 0.74         |
|  | after CPB    | 19.8               | 2.73 | 20.6                  | 4.10 | 0.87                  | 0.32         |
| [H <sup>+</sup> ] nmol / l                       | before CPB   | 37.0               | 8.32 | 38.1                  | 4.56 | 0.24                  | 0.56         |
|  | onset of CPB | 38.7               | 9.82 | 34.2                  | 4.78 | 2.20                  | 0.03         |
|  | after CPB    | 38.5               | 6.16 | 34.6                  | 5.91 | 2.76                  | 0.01         |



**Figure 1.** Dynamics of pH in groups in the perioperative period



**Figure 2.** Dynamics of potassium levels in the perioperative period

According to the analysis of the average value of ABS of blood in patients of the groups, fully compensated chronic respiratory alkalosis was revealed after induction of anesthesia. As chronic respiratory alkalosis is associated with low or normal  $\text{HCO}_3^-$  levels, and acute respiratory alkalosis is associated with high blood bicarbonate levels, a condition of chronic hypocapnia that stimulates a compensatory renal response and results in a significant decrease of  $[\text{HCO}_3^-]$  plasma [11]. At the same time, hypocapnia was more evident in the main group and significantly differed from the comparison group ( $p = 0.01$ ) (Tab. 1).

Typically, arterial pH is the measure of compensation [12]. The causes of chronic compensated respiratory alkalosis in patients with SE may have been hypoxic reasons (severe anemia, congestive heart failure, systemic infectious-inflammatory process with fever) leading to hyperventilation. After CPB, pH values move towards alkalosis in patients of the comparison group which leads to a shift of ABS towards partially compensated respiratory alkalosis. At partially compensated respiratory alkalosis, the pH buffer is almost depleted [12]. However, in the UF group, the respiratory alkalosis state remains fully compensated at this stage. In respiratory alkalosis, the compensatory reactions of the body are carried out by a decrease of bicarbonates reabsorption in the renal tubules and an increase of their excretion with the urine. As a result, the excess of buffer bases in the blood decreases, and the pH returns to the norm. [12-13]. In this state, removing bicarbonates from the blood with UF, the body's compensatory mechanism is maintained during CPB. In addition, the secretion  $[\text{H}^+]$  of ions by the kidneys decreases which is confirmed by an increase of their concentration in the blood in the main group during the onset of CPB and after CPB ( $p = 0.04$ ;  $p = 0.02$ , respectively). Another cause of respiratory alkalosis in groups during CPB is mild hypothermia ( $32^\circ\text{C}$ ), as the solubility of gases in the blood is increased at low temperatures. At the end of CPB, the pH in the main group remained within the normal range, while in the comparison group, an increase of pH ( $p = 0.005$ ) towards alkalosis was revealed (Fig. 1).

The normal pH value was maintained when using balanced UF blood in patients by improving hemoglobin, protein and bicarbonate buffering systems. After CPB, ABS indices in the balanced UF group remained in a state of complete compensation for respiratory alkalosis, in contrast to patients in the comparison group, where the compensatory buffer supply was apparently depleted (Tab. 1).

When comparing the number of patients with plasma anion gap (PAG) more than  $12 \text{ mEq/L}$  in the balanced UF group was: before CPB 7 (29%), after CPB 3 (12.5%); in the comparison group: before CPB 17 (20.2%) after CPB 7 (8.3%), with  $p > 0.05$ . An increase in PAG before surgery is often associated with: lactic acidosis, impaired renal function, with decreased glomerular filtration rate (GFR) or increased other organic anions. An increase in the anion

difference leads to a decrease in bicarbonate - the differential coefficient will be equal to one [13]. In our case, after CPB, a drop ratio equal to one was observed in 16 (66.7%) cases in the UF group and in 67 (79.7%) cases in the comparison group at  $\chi^2=1.79$ ;  $p > 0.05$ . Normal PAG values were observed in the main group: before CPB in 14 (58.3%) patients and after CPB in 17 (70.8%) patients; in the comparison group before CPB in 63 (75%) patients and after CPB in 55 (65.4%) patients with  $p > 0.05$ . Normal PAG values are estimated as compensated hyperchloremic acidosis (at preserved renal GFR). Low PAG (less than  $3 \text{ mg-eq/L}$ ) is associated with hypoalbuminemia, which can be caused by intra- and postoperative blood loss, impaired renal and liver function [10-13]. Low PAG values in the groups were significantly different: in the main group after CPB, there was no increase in the proportion of patients with this indicator (before CPB 3 (12.5%), after CPB 3 (12.5%)), in contrast to the control group where we observed an increase from 4 (4.76%) to 22 (20.1%) cases.

It is very important to assess the parameters of hemostasis, including electrolyte changes in the perioperative period, as a change in electrolyte balance leads to a change in ABS which affects metabolic processes in cells [9-10]. In our study, at assessing the average values of sodium ions in the blood, no significant differences were found between the groups ( $p > 0.05$ ). Hyponatremia before surgery did not differ statistically in the groups and made up 35% of the total number of patients ( $n = 108$ ). The first cause of hyponatremia was most likely decompensated chronic heart failure with hypervolemia of the systemic and pulmonary circulation, pulmonary hypertension and hepatomegaly.

The study of the level of potassium ions before surgery in patients with SE to assess the filtration capacity of the kidneys is very important. The groups did not statistically differ in the mean values of potassium ions during CPB ( $p = 0.79$ ). A significant difference in the mean value of blood potassium ions was observed after CPB in the UF group compared to the control group ( $p = 0.004$ ). The reason for this difference is primarily associated with the elimination of potassium ions during balanced blood UF (Fig. 2).

The dynamics of the lactate level changes did not show a significant difference between the groups in the perioperative period (main group:  $1.50 \pm 0.74 \text{ mmol/L}$ ; control group:  $1.58 \pm 0.73 \text{ mmol/L}$ ;  $p = 0.65$ ). In the main group, to eliminate the signs of anemia and maintain the proper intraoperative hematocrit values, a transfusion of  $430.2 \pm 215.5 \text{ ml}$  ( $p = 0.36$ ) of the volume of washed erythrocytes was carried out, and in order to eliminate excessive hemodilution, ultrafiltration of blood was used with the removal of fluid in an amount of  $1379, 5 \pm 810.1 \text{ ml}$  or  $22.9 \pm 15.0 \text{ ml/kg}$ . The groups did not significantly differ by the duration of artificial ventilation (main group -  $13.0 \pm 5.0 \text{ min}$ , control group -  $16.8 \pm 14.2 \text{ min}$ ,  $p = 0.218$ ), by the time spent in intensive care (main group -  $33.6 \pm 22.4 \text{ min}$ , control group -  $31.3 \pm 16.4 \text{ min}$ ,  $p = 0.699$ ), according to the duration of hospitalization (main group -  $21.9 \pm 9.1 \text{ min}$ ,

control group -  $23.6 \pm 8.8$  min,  $p = 0.442$ ). Mortality in the groups was: main group-1 (4.2%), control group-2 (2.4%),  $p > 0.05$ . Assessing the dynamics of the acid-base state, we noted that carrying out of a balanced blood UF supports compensatory mechanisms of changes in the acid-base state in patients with SE during CPB, but does not prevent the development of hyperchloremic acidosis. In our opinion, hyperchloremic acidosis developed as a result of the use of a large amount of saline sodium chloride solution during cardioplegia and directly during the surgical correction of valvular defect (washing of prolene threads, heart cavity, etc.). We used 8% Sodium bicarbonate to correct metabolic acidosis. Ryan Mullane et al. (2019), used dialysate (Z-BUF-D) to correct acidosis in cardiac surgery patients during CPB. The authors compared this group with the Z-BUF-S group where saline sodium chloride solution was used. The results showed that Z-BUF-D and Z-BUF-S significantly reduced potassium levels during CPB, but Z-BUF-D significantly reduced the need for an additional 8.4% of sodium bicarbonate [7]. X Zhu et al. conducted an advanced search to validate all Z-BUF studies. The authors were interested in clinical outcomes such as length of ICU stay, duration of ventilation, hospital stay, total chest tube drainage and mortality. In contrast to adult patients, Z-BUF reduced the duration of ALV in children. In their opinion, application of UF methods in combination can improve CPB results [8]. W A Osthaus et al. (2009) studied the effect of UF with a bicarbonate buffer as part of a priming solution on the reduction of electrolyte and acid-base balance disturbances in children during cardiopulmonary bypass. The removed UF was replaced with a buffer solution in the amount of 1000 ml. The authors concluded that this method prevented electrolyte and acid-base balance disturbances [15].

#### 4. Conclusions

In our work, we examined the changes of the acid-base state in patients with SE during CPB. It was revealed that changes in the acid-base state in patients with SE entailed changes in the electrolyte balance of the blood due to the inclusion of the compensatory systems of the body.

Balanced blood UF supports the compensatory mechanism of respiratory alkalosis in patients with SE during CPB. Balanced UF reduces hemodilution, maintains a normal level of albumin in the blood and reduces the level of potassium ions in the blood by eliminating them during filtration, which is a necessary property during hyperkalemic cardioplegia.

#### REFERENCES

[1] A. P. Medvedev, V. E. Babokin, Yu. A. Sobolev, V. V. Pichugin, V. A. Chiginev, E. N. Zemskova, N. A. Trofimov,

N. L. Blagodatkina. Modern strategy in the surgical treatment of destructive forms of infective endocarditis. *Creative surgery and oncology*. Volume 8, No. 2 (2018) <https://doi.org/10.24060/2076-3093-2018-8-2-10-18>.

- [2] Matthieu Legrand, Romain Pirracchio, Anne Rosa, Maya L Petersen, Mark Van der Laan, Jean-Noël Fabiani, Mariepaule Fernandez-gerlinger, Isabelle Podglajen, Denis Safran, Bernard Cholley, Jean-Luc Mainardi. Incidence, risk factors and prediction of post-operative acute kidney injury following cardiac surgery for active infective endocarditis: an observational study *Crit Care*. 2013; 17(5): R220. Published online 2013 Oct 4. doi: 10.1186/cc13041.
- [3] Kornilov I.A., Ponomarev D.N., Shmyrev V.A., Skopets A.A., Sinelnikov Yu.S., Lomivorotov V.V. Physiological parameters of artificial blood circulation from the point of view of evidence-based medicine. *Bulletin of Anesthesiology and Reanimatology*, Volume 13, No. 3, 2016.
- [4] Kun Zhang, Lishen Wang\* and Shuwei Shen. Ultrafiltration Technology and Its Application in Cardiopulmonary Bypass. *MATEC Web of Conferences* 100 GCM 2016, DOI: 10.1051/(2017) 710003027.
- [5] Mick S, Hilberath J, Davidson M, FitzGerald D. Zero balance ultrafiltration for the correction of acute acidosis after a period of prolonged deep hypothermic circulatory arrest. *Perfusion*. 2011; 27(1): 9–11.
- [6] Mohsen Ziyaeifard, Azin Alizadehasl, Nahid Aghdaii, Poupak Rahimzadeh, Gholamreza Masoumi, Samad EJ Golzari, Mostafa Fatahi, Farhad Gorjipur. The effect of combined conventional and modified ultrafiltration on mechanical ventilation and hemodynamic changes in congenital heart surgery. *J Res Med Sci*. 2016; 21: 113. Published online 2016 Nov 7. doi: 10.4103/1735-1995.193504 [PubMed].
- [7] Mullane R, Fristoe L, Markin NW, Brakke TR, Merritt-Genore HM, Siddique A, Miles CD, Zero balance ultrafiltration using dialysate during nationwide bicarbonate shortage: a retrospective analysis. *Plumb TJJ Cardiothorac Surg*. 2019 Sep 10; 14(1): 163. doi:10.1186/s13019-019-0986-8. PMID: 31500645 [PubMed].
- [8] Zhu X, Ji B, Wang G, Liu J, Long C. The effects of zero-balance ultrafiltration on postoperative recovery after cardiopulmonary bypass: a meta-analysis of randomized controlled trials. *Perfusion*. 2012; 27(5): 386–392. doi: 10.1177/0267659112450182. - DOI - PubMed.
- [9] Robin Peter Alston. Metabolic acidosis developing during cardiopulmonary bypass is related to a decrease in strong ion difference *Perfusion* 19(3): 145-52 2004 DOI:10.1191/0267659104pf751oa [PubMed].
- [10] Kostyuchenko S. S. Acid-base balance in intensive care: Minsk, 2009. 268 p.: <https://www.bibliofond.ru/view.aspx?id=817764>.
- [11] Batlle D, Chin-Theodorou J, Tucker BM. Metabolic Acidosis or Respiratory Alkalosis? Evaluation of a Low Plasma Bicarbonate Using the Urine Anion Gap. *Am. J. Kidney Dis*. 2017 Sep; 70(3): 440-444. [PubMed].
- [12] Morrison V.V., Chesnokova N.P., Bizenkova M.N. Acid-base state Regulation of acid-base homeostasis (Lecture 1). // *International Journal of Applied and*

Fundamental Research. 2015. No. 3-2. P. 270-273; URL: <https://applied-research.ru/ru/article/view?id=652>.

- [13] Fidkowski, C And J. Helstrom. Diagnosing metabolic acidosis in the critically ill: bridging the anion gap, Stewart and base excess methods. *Can J Anesth* 2009; 56: 247-256.
- [14] Haase M, Haase-Fielitz A, Bellomo R, Devarajan P, Story D, Matalanis G, Reade MC, Bagshaw SM, Seevanayagam N, Seevanayagam S, et al. Sodium bicarbonate to prevent increases in serum creatinine after cardiac surgery: a pilot double-blind, randomized controlled trial. *Crit Care Med.* 2009; 37(1): 39–47. doi: 10.1097/CCM.0b013e318193216f.
- [15] W A Osthaus, H Görler, J Sievers, N Rahe-Meyer, J Optenhöfel, T Breymann, G Theilmeier, R Suempelmann. Bicarbonate-buffered ultrafiltration during pediatric cardiac surgery prevents electrolyte and acid-base balance disturbances. *Perfusion* 2009 Jan; 24(1): 19-25. doi: 10.1177/0267659109106728 [PubMed].

Copyright © 2020 The Author(s). Published by Scientific & Academic Publishing

This work is licensed under the Creative Commons Attribution International License (CC BY). <http://creativecommons.org/licenses/by/4.0/>