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A new look at the correction of COVID-19-mediated pulmonary gas exchange disorders

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Abstract

Aim. To assess the effect of meglumine sodium succinate on the effectiveness of basic therapy in correcting gas exchange abnormalities in patients with severe COVID-19 infection complicated by bilateral community-acquired pneumonia.

Methods. The analysis of the effectiveness of therapy of 12 patients with a diagnosis of "New coronavirus infection COVID-19 (confirmed), severe form U07.1. Complication: bilateral multifocal pneumonia" was carried out. The patients were divided into two groups: 7 received, as part of standard therapy, a solution of meglumine sodium succinate in a daily dose of 5 ml/kg during stay in the intensive care unit; 5 patients received a similar volume of Ringer's solution and formed the control group. In the arterial and venous blood of all patients, the indicators of acid-base state and water-electrolyte balance, glycemia and lactatemia were measured at several stages: (1) at admission to the intensive care unit, (2) 2–4 hours after the start of intensive therapy, (3) after 8–12 hours, (4) after 24 hours. On the 28th day of observation, mortality, the duration of treatment in the intensive care unit and the incidence of thrombotic complications in the groups were assessed. The Friedman nonparametric hypothesis test was used to assess intragroup dynamics, and the nonparametric Mann–hitney U test for intergroup comparisons.

Results. In the group of patients who received meglumine sodium succinate, there was a significant decrease in the incidence of thromboembolic events during 28 days of treatment: myocardial ischemia event rate ratio from 0.89 [95% confidence interval (CI) 0.19–1.16] in the control group to 0.55 (95% CI 0.06–0.81) in the study group at p=0.043; pulmonary embolism event from 0.50 (95% CI 0–1.0) in the control group to 0.28 (95% CI 0–1.0) in the study group at p=0.041. There was also a decrease in the duration of intensive care unit length of stay to 6.1±1.1 days in the study group versus 8.9±1.3 days in the control group.

Conclusion. Compared with standard infusion therapy, the use of meglumine sodium succinate leads to a faster normalization of ventilation-perfusion ratios in patients with severe coronavirus infection.

Keywords: coronavirus infection, COVID-19, endothelium, meglumine sodium succinate.

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Background. From the moment of receiving the first information about the new coronavirus (COVID-19) infection and up to the present, the predominant damage to the respiratory tract with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viruses remains the main link of the disease pathogenesis [1]. First of all, this is due to the most common route of virus invasion through binding to angiotensin-converting enzyme 2, which is expressed on epithelial and endothelial cells of the respiratory tract and some other cell types, due to the presence of two important regions of the S-protein in SARS-CoV-2 (S1 and S2), which determine the contagiousness of the virus [2].

The above data are confirmed pathoanatomically. Most authors in their works demonstrate bilateral diffuse alveolar lesion of the lungs with exudation, desquamation of pneumocytes and

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hyaline membranes, edema, interstitial lymphocytic inflammatory infiltrates, and vascular lesions of the lungs in the form of widespread microthrombi in the pulmonary capillaries [3–5].

Such a rapid and massive damage to the structures of the alveolocapillary membrane and the endothelium of the pulmonary vessels in severe cases leads to the low efficiency of various strategies of artificial lung ventilation and often requires extracorporeal oxygenation. At the same time, the relationship between the increasing severity of disturbances in gas exchange, acid-base state (ABS), and water-electrolyte balance (WEB) and survival in patients with the new coronavirus infection has been demonstrated in several works [6–8].

As the researchers show, the timely use of antiviral, anti-inflammatory, and anticoagulant therapy for the new coronavirus infection helped reduce its severity. However, the effectiveness of these therapeutic measures in optimizing impaired gas exchange, especially in severe cases, is still far from perfect. Thus, further research for new organ-protection strategies that can prevent or significantly reduce the severity of COVID-related epithelial and endotheliopathies is required.

Earlier, the use of meglumine sodium succinate (reamberin) in various types of respiratory hypoxia has shown optimistic results. In particular, it was found to significantly improve the gas exchange of patients with infectious destruction of the lungs [9], respiratory failure in postpartum sepsis [10], acute respiratory distress syndrome against the background of acute poisoning with drugs such as methadone and azaleptin [11, 12] and against the background of severe pancreatitis with the rapid and significant drug effect on the normalization of the functional lung state in severe endotoxicosis [13].

The authors in the clinic and experiment have shown that, regardless of the prevailing etiological factor, as a result of an increase in the energy potential, primarily of endothelial cells in direct contact with the antihypoxant after its parenteral administration, the permeability of their membranes is normalized and the activity of necrobiotic processes decreases, which generally reduces the severity of endothelial dysfunction at various critical states [14–16]. We have not found any studies in which the intensity of COVID-mediated disturbances in gas exchange, ABS, and WEB was corrected by infusing antihypoxant.

This study aimed to evaluate the effect of meglumine sodium succinate on basic therapy in correcting gas exchange disorders in patients with severe COVID-19 infection complicated by bilateral community-acquired pneumonia.

Material and methods. The pilot study included 12 patients diagnosed with COVID-19 infection (confirmed by polymerase chain reaction [PCR]), severe form U07.1, and bilateral polysegmental pneumonia complication who were treated at City Clinical Hospital No. 30 (Nizhny Novgorod) from April to September 2020. All patients admitted to the intensive care unit (ICU) had an initial severity of 4–6 points on the English National Early Warning Score (NEWS) scale without the need for invasive mechanical ventilation.

The control group consisted of five patients who received standard therapy. The study group consisted of seven patients who, with the approval of the medical commission of City Clinical Hospital No. 30, received a 1.5% solution of meglumine sodium succinate at a dose of 5 mL/kg intravenously for 2 h every day during the entire ICU stay period as a part of standard therapy for WEB correction and detoxification.

The randomization was carried out following a pregenerated table of random numbers linked to the medical record number.

In the control group, the infusion therapy volume was similar. The administration dose could always be adjusted based on clinical efficacy, individual drug tolerance, and laboratory results in each specific case; however, no correction was required for patients included in the study.

To prevent thrombotic complications, all examined patients were given 5000 IU of unfractionated heparin intravenously thrice a day during the entire ICU stay. All patients received the same etiotropic and pathogenetic therapy following the current temporary guidelines of the Ministry of Health of the Russian Federation. It included favipiravir, barcitinib, heparin, nonsteroidal anti-inflammatory drugs according to indications, and levofloxacin, as well as drugs for treating concomitant diseases (according to indications).

The inclusion criteria of the study are as follows:

1) diagnosis of COVID-19 (established based on clinical data and subsequently confirmed by PCR) and a severe form complicated by the development of bilateral community-acquired pneumonia (according to computed tomography);

2) disease duration of no more than 3 days;

3) ICU hospitalization within the first 4 h after admission;

4) time between diagnosis establishment and study inclusion is no more than 24 h;

5) age between 18 and 75 years;

6) an initial severity of 4–6 points on the NEWS scale;

7) lack of evidence of simultaneous intake of antioxidant and antihypoxic drugs.

Table 1. Demographic and Clinical Data of Treatment Groups

Criterion	Control group (min; max)	Test group (min; max)	p
Number of patients	5	7	—
Male sex, abs. (%)	3 (60.0)	5 (71.4)	0.75
Average age (years)	61 [40; 73]	57 [38; 70]	0.89
Baseline NEWS score (range)	5.2 [4; 6]	5.5 [4; 6]	0.88
Heart failure (NYHA), median (range)	2 [1; 4]	2 [1; 4]	0.89
Arrhythmias, abs. (%)	1 (20.0)	2 (28.6)	0.81
Type 2 diabetes mellitus, abs. (%)	2 (40.0)	3 (42.9)	0.74
Concomitant chronic obstructive pulmonary disease, abs. (%)	1 (20.0)	1 (14.3)	0.87
Body mass index over 30.0 kg/m^2, abs. (%)	2 (40.0)	3 (42.9)	0.74
Lung damage volume according to computed tomography, points (%)	3 (80) 4 (20)	3 (85.7) 4 (14.3%)	0.81

NEWS (from the English National Early Warning Score) is a scale used to assess the severity of the condition. NYHA (from the English New York Heart Association) is a classification of the New York Heart Association.

The exclusion criteria are the following:

1) the presence of early established oncological diseases;

2) an infection caused by the human immunodeficiency virus;

3) pregnancy;

4) the presence of concomitant chronic diseases in the decompensation stage;

5) drug intolerance;

6) patients' unwillingness to remain in the study;

7) iatrogenic complications of intensive care;

8) lack of confirmation of the pathogen after two PCR tests.

The study and control groups were compared in terms of gender and age, initial severity of the condition, and presence in the anamnesis of diseases such as heart rhythm disturbances, ischemic heart disease, heart failure, and hypertension (Table 1).

Daily monitoring was performed following the requirements of the Harvard standard. The studies of ABS and WEB parameters, as well as glucose and lactate, were performed on an automatic ABS and WEB analyzer GEM Premier 3000 (China**)**. The study was carried out within 15 min from the moment of blood sampling. Complete blood count was performed on an automatic analyzer Mindray BC-5380 (China). The following parameters were measured in the arterial and venous blood of patients taken simultaneously from the ulnar vein and femoral artery: pH, carbon dioxide (pCO_2) and oxygen (pO_2) voltages, base deficiency (BD), glucose and sodium levels, potassium, and lactate. The arteriovenous difference in the values of pCO_2 and pO_2 voltages was calculated.

The collection of arterial and venous blood was carried out in four stages: the 1st stage was upon admission to the ICU from the emergency room while breathing in atmospheric air; the 2nd stage was 2–4 h after the completion of primary infusion therapy and administration of the first heparin dose; the 3rd stage was 8–12 h after the completion of primary infusion therapy and administration of a repeated heparin dose; the 4th stage is 24 h after the start of intensive therapy.

The study evaluated the speed of coagulopathy correction against the background of anticoagulant therapy in the prophylactic dose regimen (reaching the activated partial thromboplastin time level + 50% of the norm, reducing the concentration of D-dimers, correcting hyperfibrinogenemia, and normalizing platelet levels).

The primary endpoint is the number of adverse thrombotic complications, the length of ICU admission, and 28-day mortality. Unfavorable thromboembolic complications were stroke (according to the American College of Surgeons National Surgical Quality Improvement Program), arterial thrombosis diagnosed according to standard criteria, pulmonary embolism, and myocardial infarction. Data were collected within 24 h of admission (transfer) to the ICU of a COVID hospital at the four fixed points identified in the study, as well as on the 28th day of inpatient treatment.

Statistical data processing was performed in the IBM SPSS v. 23. The scale of the analyzed data is absolute. To assess the significance of shifts in the functional state of operators, considering the division into groups, the following analysis parameters were selected. A nonparametric analysis of variance with the Friedman test was used to assess intragroup dynamics. Related samples were obtained initially and in 2–4 h, 8–12 h, and 24 h.

A posteriori comparison was performed using the Tukey test if the variances of the compared features were equal or the Games–Howell test if this condition was unmet. For intergroup comparisons, the nonparametric Mann–Whitney *U* test was used. During the simultaneous testing of several hypotheses (six indicators using the Friedman test and four gradations of each indicator for paired comparisons), the Benjamini–Hochberg correction for multiple comparisons was applied. The significance level at which the null hypothesis was rejected was $p < 0.05$. With a value of $0.05 \leq p \leq 0.1$, a statistical trend was determined. The description of the data and their variance were of the form Me (Q_{25}; Q_{75}), where Me is the median and Q_{25} and Q_{75} are the 25% and 75% quartiles, respectively.

Results and discussion. A generalized analysis of the dynamics of laboratory parameters characterizing ABS and WEB indicates that arterial blood reacts to the use of an infusion antihypoxant and is more pronounced and faster than venous blood. Thus, in the absence of significant pH dynamics in the venous blood of patients against the background of various infusion therapies, the analysis of a similar indicator in the arterial blood showed that, against the background of the initiation of standard infusion therapy, the initially increased indicator decreased. At the same time, at the 3rd stage of the study (8–12 h after the start of therapy), the pH in arterial blood in patients from the control group was significantly lower than both the initial values and those similar in the study group ($U = 0$, $Z = -2.87$, $p_{corr} = 0.016$; Fig. 1). Thus, the use of meglumine sodium succinate made it possible to avoid an episode of initial reperfusion acidosis in arterial blood at all stages of follow-up.

Thus, the expected effect of using an infusion antihypoxant is mainly in the stabilization of the pH in arterial blood against the background of the initiation of basic treatment, which initiated an episode of acidity increase in comparison with traditional therapy.

Changes in the BD of venous and arterial blood against the background of various regimens of infusion therapy repeat the dynamics of the above-described changes in ABS; however, they are more pronounced and changing at all stages of the study (Fig. 2).

The initially increased level of BD decreases in both groups against the background of the initiation of basic therapy. At the same time, if the infusion of meglumine sodium succinate, accompanied by pH stabilization, in the early postinfusion period also led to a stable normalization of the BD index, then the standard infusion therapy required

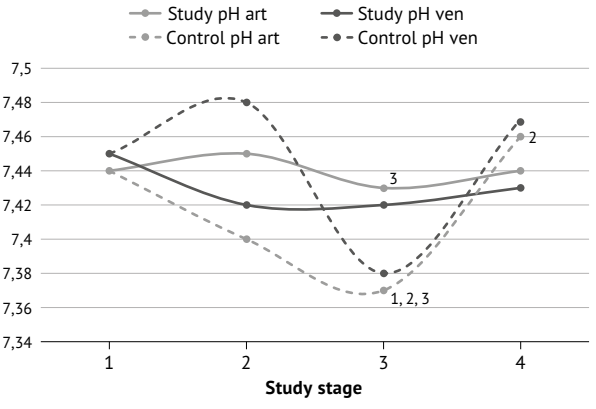

Fig. 1. Hydrogen index (pH) of arterial and venous blood against the background of various regimens of infusion therapy, −log10. (1) Significant difference relative to the initial data ($p < 0.05$); (2) significant difference from the previous stage of the study ($p < 0.05$); (3) significant intergroup difference ($p < 0.05$). Study, study group; Control, control group; art, arterial blood; veins, venous blood.

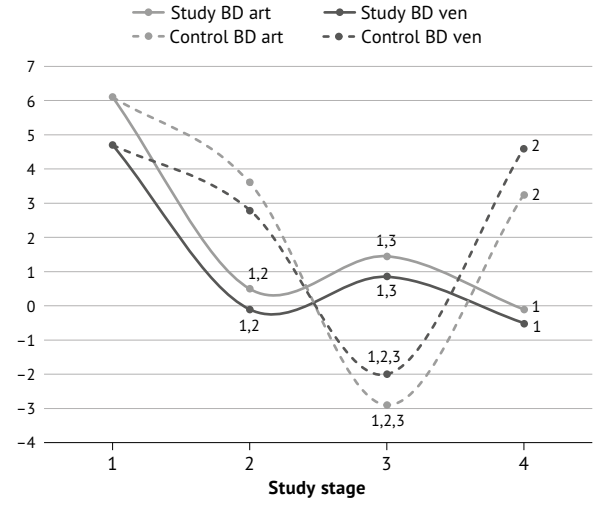

Fig. 2. Base deficiency (BD, mmol/L) of arterial (art) and venous (ven) blood on the background of various regimens of infusion therapy. (1) Significant difference relative to the initial data ($p < 0.05$); (2) significant difference from the previous stage of the study ($p < 0.05$); (3) significant intergroup difference ($p < 0.05$). Study, study group; Control, control group.

compensation for the increasing acidotic changes in the blood plasma, especially by the 3rd stage of the study. This was accompanied by an increasing BD, which characterizes both the direction of the dynamics of changes in ABS and the degree of their compensation against the background of standard infusion therapy. At the same time, the most significant intergroup difference in the level of DO at the 3rd stage of the study was noted in arterial blood, where it reached $U_{8–12\,h} = 2.0$, $Z = -2.52$, $p_{corr.} = 0.024$; $U_{24\,h} = 0$, $Z = -2.84$, $p_{corr.} = 0.018$.

Thus, the effect of the infusion of meglumine sodium succinate mainly lies in the stability of the

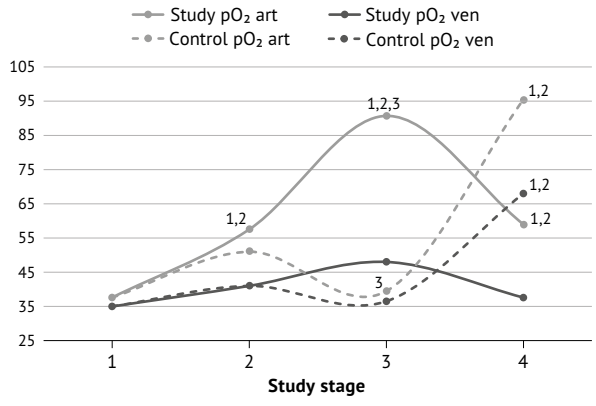

Fig. 3. Arterial blood oxygen tension (pO2) of arterial and venous blood against the background of various regimens of infusion therapy (mmHg). (1) Significant difference from the initial data ($p < 0.05$); (2) significant difference from the previous stage of the study ($p < 0.05$); (3) significant intergroup difference ($p < 0.05$). Study, study group; Control, control group; art, arterial blood; veins, venous blood.

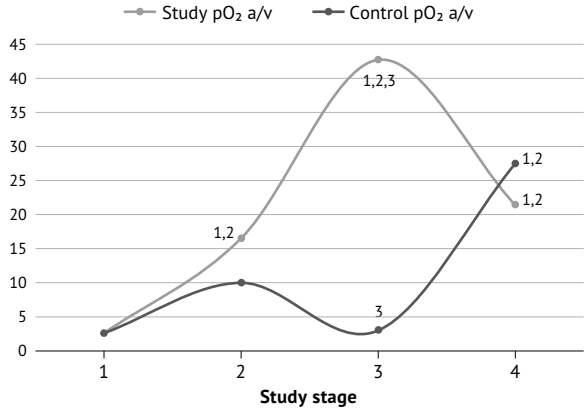

Fig. 4. Arteriovenous difference in oxygen tension (pO2) of blood against the background of various schemes of infusion therapy (mmHg). (1) Significant difference from the initial data ($p < 0.05$); (2) significant difference from the previous stage of the study ($p < 0.05$); (3) significant intergroup difference ($p < 0.05$). Study, study group; Control, control group; a/v, arterial/venous blood.

correction of changes in the BD index than that of traditional infusion therapy.

We believe that, in addition to respiratory causes, possible additional factors contributing to the formation of the above phenomenon of metabolic alkalosis against the background of hypercapnia in the studied patients may be the described early phenomenon of hypercompensation of lactic acidosis and initial ketosis in patients with diabetes mellitus (also included in the groups).

The presence of pronounced alkalosis on admission, with low levels of dissolved oxygen and high carbon dioxide of lactate in patients with the new coronavirus infection, was also recorded in other studies. Moreover, the severity of the initial alkalosis was correlated with mortality [17].

The dynamics of the pO_2 index corresponds to the trends in changes in ABS against the background of various regimens of infusion therapy (Fig. 3).

Initially, extremely low values of the indicator, both in arterial and venous blood, with a minimal arteriovenous difference; characterize the initial severity of impaired pulmonary gas exchange against the background of severe bypass surgery, updated with a minimum anoxic respiratory interval. The pronounced oxygen debt does not completely stabilize this situation, even against the background of a 2-h high-flow inhalation.

At the same time, a significant increase in this indicator was found against the background of the infusion of meglumine sodium succinate starting from the 2nd stage of the study ($\chi^2 = 15.86$, $p_{corr.} < 0.01$), which, together with its stable level in the venous blood at all stages of the study, led to a significant increase in the arteriovenous difference in the 2nd and 3rd stages of the study (Fig. 4).

Against the background of standard infusion therapy, we also noted an increase in the oxygen tension indicator; however, it occurred more delayed (at the 4th stage), was accompanied by a synchronous increase in its venous content without an increase in the extraction level, and also had a significantly lower severity compared with the dynamics of the control group ($\chi^2 = 9.24$, $p_{corr.} = 0.092$).

It should be noted that no significant intergroup differences were revealed at the end of the study, whereas the arterial blood index in the study group was significantly higher against the background of using meglumine sodium succinate at the 3rd stage ($U = 0$, $Z = -2.84$, $p_{corr.} = 0.018$).

Improvement of pulmonary gas exchange, as well as activation of metabolic processes in tissues against the background of using an infusion of a substrate antihypoxant, naturally affected the change in the arteriovenous difference in oxygen tension at the stages of treatment (Fig. 4). Despite the unidirectional changes, the achievement of such a significant antihypoxic effect as an increase in oxygen saturation of arterial blood, together with the acceleration of its utilization, was faster and more pronounced in the study group, already starting from the 2nd stage of the study. Thus, the effect of using meglumine sodium succinate on the level of pO_2 in the blood plasma mainly lies in the speed of the onset of the effect of the basic treatment compared with standard therapy.

The dynamics of pCO_2 at the stages of treatment are shown in Fig. 5. On the background of meglumine sodium succinate infusion, a rapid and significant decrease in the initially elevated pCO_2 index in arterial blood was noted, starting from the 2nd stage of the study ($\chi^2 = 13.14$, $p_{corr.} = 0.021$). A simi-

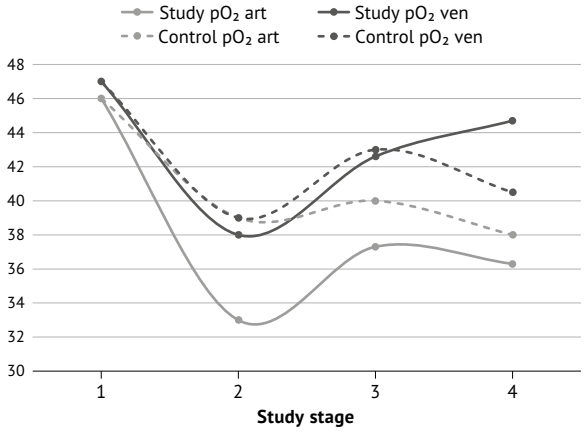

Fig. 5. Carbon dioxide tension (pCO2) of arterial and venous blood on the background of various regimens of infusion therapy (mmHg). (1) Significant difference from the initial data ($p < 0.05$); (2) significant difference from the previous stage of the study ($p < 0.05$); (3) significant intergroup difference ($p < 0.05$). Study, study group; Control, control group; art, arterial blood; ven, venous blood.

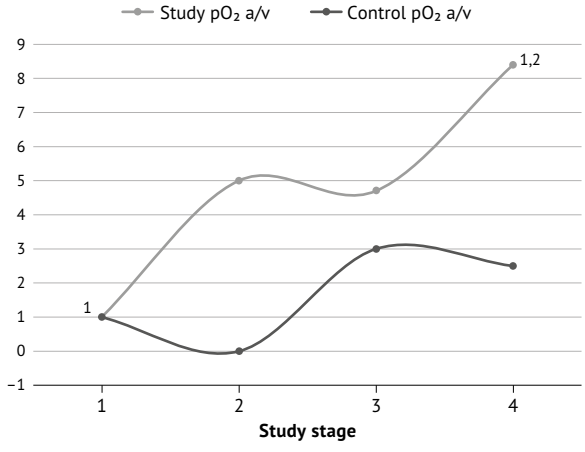

Fig. 6. Arteriovenous difference in blood carbon dioxide (pCO2) voltage on the background of various infusion therapy regimens (mmHg). (1) Significant difference from the initial data ($p < 0.05$), (2) significant difference from the previous stage of the study ($p < 0.05$), (3) significant intergroup difference ($p < 0.05$). Study, study group; Control, control group; a/v, arterial/venous blood.

lar trend was recorded against the background of standard therapy, but it was much less pronounced and did not achieve significant differences until the end of the study.

At the same time, the dynamics of a similar indicator in the venous blood in both study groups did not differ significantly, which naturally led to multidirectional changes in the arteriovenous difference in the control and study groups (Fig. 6). The use of meglumine sodium succinate, having a positive effect on the dynamics of the parameters of the partial pressure of oxygen in arterial blood, discussed above, as well as on its utilization, naturally led to a significant increase in the arteriovenous pCO_2 difference in blood plasma, exceeding the initial level by an average of 12.4% already after 1 day of intensive therapy, whereas no changes in this indicator were observed during the study against the background of standard infusion therapy.

The most pronounced effect of meglumine sodium succinate infusion on electrolyte balance was observed in the analysis of intergroup differences in venous blood plasma potassium concentration (Fig. 7). The use of an infusion antihypoxant in comparison with traditional infusion therapy makes it possible to avoid a postinfusion increase in hyperkalemia, and a generalized analysis of the dynamics of this indicator demonstrates the significance of intergroup differences reaching maximum values at the 2nd stage of the study. At the same time, considering the sample size, post-hoc tests reduce the significance of differences at this stage to $\chi^2 = 8.75$, $p_{corr.} = 0.077$.

The antihypoxic nature of the effect of the infusion used in the study group is confirmed by inter-

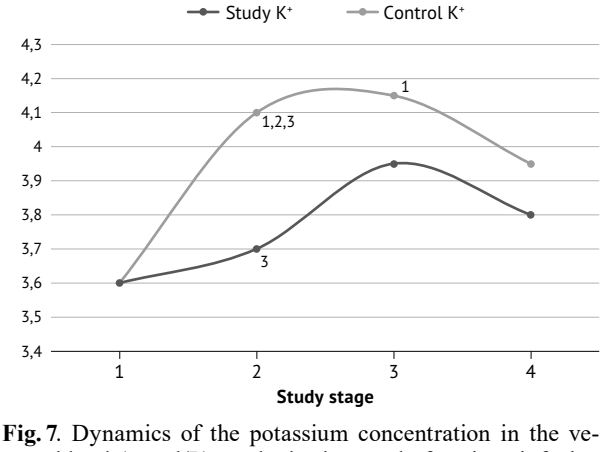

Fig. 7. Dynamics of the potassium concentration in the venous blood (mmol/L) on the background of various infusion therapy regimens. (1) Significant difference from the initial data ($p < 0.05$); (2) significant difference from the previous stage of the study ($p < 0.05$); (3) significant intergroup difference ($p < 0.05$). Study, study group; Control, control group

group differences in the plasma dynamics of lactate and glucose. Thus, the initially elevated glycemic level in the groups, averaging 10.5 ± 1.46 mmol/L, was quickly corrected against the background of the antihypoxant infusion and was 7.6 ± 2.45 mmol/L at the 2-h follow-up stage. Then, against the background of standard therapy, there was a directly opposite trend as the indicator increased to 10.8 ± 0.81 mmol/L ($p = 0.12$), and up to 12 ± 1.31 mmol/L ($p = 0.11$) by the 8 h, while maintaining the above tendency up to 24 h of observation (Table 2).

The tendency noted above for the correction of hyperglycemia was accompanied by a similar dynamic in the lactate level in the blood plasma. Thus, the initial lactatemia, which averaged

Table 2. Dynamics of the concentration of glucose, sodium, and lactate in venous blood against the background of various regimens of infusion therapy

Group	Parameter (mmol/L)	Time from end of meglumine sodium succinate infusion			
		Baseline	2 h	8 h	24 h
Control	Glucose	10.5±1.46	10.8±0.81	12±1.31	14.8±4.27
	Na^+	142±3.38	142±1.03	140±3.65	142.6±1.66
	Lactate	1.8±0.21	1.8±0.78	2±0.16	1.82±0.27
Study	Glucose	10.5±1.46	7.6±2.45	8.7±1.82	10.0±2.05
	Na^+	142±3.38	139.7±1.57	142.7±3.29	140.8±3.56
	Lactate	1.8±0.21	1.9±0.62	1.6±0.29	1.6±0.40

1.8 ± 0.21 mmol/L, against the background of using antihypoxant, quickly corrected at the stage of 8-h observation to 1.6 ± 0.29 mmol/L. Meanwhile, against the background of standard therapy, it was the opposite tendency as the indicator increased to 2.0 ± 0.16 mmol/L (p = 0.33), with the preservation of the pattern up to 24 h of observation (Table 2).

Analysis of the disease course and its outcomes on the 28th day of participation in the study showed that the inclusion of meglumine sodium succinate in the therapy regimen did not increase the chances of a favorable outcome: mortality was 2 (28.6%) patients in the study group and 1 (20.0%) case in the control group (p = 0.84). However, this difference cannot be interpreted because of the small number of groups represented. On the other hand, the use of the drug reduced the risks of thromboembolic events in patients within 28 days of treatment: episodes of myocardial ischemia from 0.89 (95% confidence interval [CI] 0.19–1.16) in the control group to 0.55 (95% CI 0.06–0.81) in the study group (p = 0.043) and pulmonary embolism from 0.50 (95% CI 0–1.0) in the control group to 0.28 (95% CI 0–1.0) in the study group (p = 0.041). In the group that received meglumine sodium succinate, there was a decrease in the ICU stay duration: 6.1 ± 1.1 days in the study group *versus* 8.9 ± 1.3 days in the control group.

The results obtained, characterized by the acceleration of the normalization of impaired gas exchange and ABS, generally correspond to the earlier published data on the use of meglumine sodium succinate in hypoxic conditions of various origins. In particular, Fufaeva et al. (2007) studied the effect of meglumine sodium succinate on the oxygen homeostasis indicators (arteriovenous oxygen tension difference) in 87 patients with respiratory failure as a result of acute infectious destruction of the lungs and noted that it activated metabolic processes as it increased the difference of pO2 in arterial and venous blood [9]. According to the research results of Yakovleva et al. (2011), patients with postpartum sepsis receiving the study drug showed an increase in the oxygenation index earlier than in the control group, as well as an earlier completion of mechanical ventilation [10].

Also, meglumine sodium succinate has successfully established itself as a drug that reduces signs of hypoxia, acute respiratory distress syndrome, and acute respiratory failure and lowers the duration of mechanical ventilation in patients with acute poisoning with drugs such as methadone and azaleptin [11, 12]. Vlasova et al. (2012) observed the stabilization of the gas composition of blood and ABS against the background of using meglumine sodium succinate in pancreatitis [13]. The authors showed a rapid and significant effect of the drug on the normalization of the functional lung state.

One of the most probable mechanisms for the implementation of the antihypoxic effects of succinates, the authors call an increase in the energy potential, primarily of endothelial cells, which are in direct contact with the antihypoxant after its parenteral administration, which normalizes the permeability of their membranes, reduces the activity of various necrobiotic processes, and generally reduces the severity of endothelial dysfunction at various states [14–16].

The tendency to improve pulmonary gas exchange rates demonstrated in this study against the background of a single meglumine sodium succinate infusion led to regular changes in the ABS and WEB parameters, which in turn correlated with the results of treatment of the new coronavirus infection in general. Also, although data on the relationship between ABS and WEB disorders with the effectiveness of intensive care and survival in patients with COVID-19 are still limited, this is also confirmed in a number of sources.

Thus, Bezuidenhout et al. (2020), when assessing the correlation of ABS and blood electrolytes with the disease outcome, noted that the mean values of pH, pO_2, HCO_3, and BD were higher in the surviving patient group, but statistically significant differences were noted only in relation to pH and pO2 in arterial blood. Researchers have identified

an elevated pH as a predictor of survival. The mean levels of potassium, sodium, lactate, creatinine, and urea in the groups of surviving and deceased patients did not differ statistically [6].

In a small study, Zhang et al. (2020) evaluated the blood gas data of 20 patients who required mechanical ventilation. The authors compared the indicators before and after mechanical ventilation and found that seven deceased patients had a statistically significant increase in lactate content compared with survivors [7].

Conclusion. The findings from a pilot study on correcting gas exchange disorders associated with COVID-19 lung damage are cautiously optimistic. It was noted that the use of meglumine sodium succinate significantly reduced the risks of thromboembolic events in patients within 28 days of treatment and also led to a decrease in ICU stay duration. Patients in this group responded more quickly to basic therapy, which was expressed in a more distinct positive dynamics of impaired indicators of ABS and WEB, as well as markers of hypoxia (lactatemia and glycemia). As a possible explanation of the results obtained, it can be assumed that the metabolic effect of succinate increases the resistance of the endothelium and epithelium of lung tissues and lung vessels to the action of damaging factors, which in general reduces the severity of changes in the alveolocapillary membrane and leads to the normalization of ventilation-perfusion ratios.

The pilot format of the study (a sample of 12 patients) does not allow concluding the effectiveness of the drug on mortality: the groups did not have a statistically significant difference in this indicator (28.6% and 20.0%, $p = 0.84$).

This study is the first to use meglumine sodium succinate in patients with the new coronavirus infection, indicating that a substrate antihypoxant infusion in patients with this pathology seems promising. The hypothesis requires testing an extended clinical study with a design that includes a laboratory assessment of the effectiveness of different course doses of the study drug and differentiating the mechanism of antihypoxant effect on specific structures of the alveolocapillary membrane.

CONCLUSION

The use of meglumine sodium succinate compared with standard infusion therapy leads to a more rapid normalization of ventilation-perfusion ratios in patients with severe coronavirus infection.

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