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## ANALYSIS OF BLOOD GAS COMPOSITION INDICATORS IN PREMATURE BABIES WITH NEONATAL SEPSIS

O. Vlasova, L. Kolyubakina

**Мета роботи** – аналіз показників кисневого статусу хворих на неонатальний сепсис під час моніторингу стану передчасно народжених немовлят.

**Матеріали та методи.** Показники кисневого статусу капілярної крові були оцінені у передчасно народжених немовлят, хворих на неонатальний сепсис, які знаходились на лікуванні в Обласному перинатальному центрі м. Хмельницького впродовж 2017–2018 років. В дослідження увійшли переважно глибоко недоношені діти, у тому числі з екстремально низькою вагою. Проведено повний комплекс клінічно-лабораторних досліджень, в тому числі визначення показників кисневого статусу капілярної крові.

**Результати досліджень.** Отримані результати дозволяють зробити висновок, що в той час, поки такі показники як рН, рO<sub>2</sub>, BE<sub>3</sub>, %SO<sub>2</sub> помітно не змінюються, неблагополуччя можна виявити за допомогою таких показників, як AdDO<sub>2</sub>, RI, PI, які відображають стан оксигенації з порушенням вентильційно-перфузійних співвідношень, посиленням шунтування крові та процесів доставки та споживання кисню на рівні тканин. Розрахований показник «PIP×FiO<sub>2</sub>» виявився менш чутливим для оцінки змін зі сторони легень та не відповідав клінічній картині тяжкості стану пацієнтів.

**Висновок.** Таким чином визначення показників AdDO<sub>2</sub>, RI, PI капілярної крові можна використовувати в якості інформативних показників визначення кисневого статусу у передчасно народжених немовлят, що має суттєве практичне значення в умовах обмежених можливостей моніторингу газового складу артеріальної крові

**Ключові слова:** неонатальний сепсис, передчасно народжені діти, показники кисневого статусу, респіраторний індекс

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### 1. Introduction

Newborns who are in a serious condition, quite often get disorders of vital functions of the body, which are embedded in the concept of systemic inflammatory response syndrome. The universality of the development of a systemic inflammatory response with an uncontrolled cascade of cytokine-mediator reactions leads to the formation of multiorgan failure syndrome [1–3]. Assessment of the severity of organ disorders, dynamic monitoring of the patient's condition and the need for correction of therapeutic measures in neonatal sepsis is one of the important tasks in predicting both the immediate and long-term consequences of the disease. The number of scales for assessing organ insufficiency proposed today for newborns [4–6] are based mainly on clinical and laboratory criteria of organ disorders. Assessment of respiratory dysfunction and hemostasis is based on information about the main aspects of oxygen metabolism in the body, i. e. the determination of oxygen status, namely, indicators that reflect the absorption of oxygen by the lungs, its transport by blood and return to tissues. One of the key tasks is to obtain a sample of whole arterial blood of infants, which requires systematic monitoring of the dynamics. However, the risk of complications in arterial blood collection in this category of patients exceeds the feasibility of its use [7–9]. A review of the literature [9, 10] confirms that capillary blood pa-

rameters can be used to assess the oxygen status of premature infants. The composition of capillary blood reflects not only the function of the lungs, but also associated with the processes of delivery and consumption of oxygen to tissues.

The study included premature infants with neonatal sepsis, as this category of infants mainly determines the rates of infant morbidity and mortality, despite the use of modern perinatal technologies in the field of care and treatment.

**The aim of the research** – analysis of oxygen status of patients with neonatal sepsis during monitoring of premature infants.

### 2. Materials and methods

Indicators of the oxygen status of capillary blood were assessed in 17 premature infants with neonatal sepsis who were treated at the Regional Perinatal Center in Khmelnytsky during 2017–2018. The study included mostly preterm infants, including those with extremely low birth weight, as this category of infants is a high-risk group for adverse disease and disability. The diagnosis of sepsis was established according to clinical and diagnostic signs and determination of the level of the marker of presepsin in the serum [12, 13].

All newborns were on long-term traditional artificial lung ventilation in A/C mode. The volume of exam-

inations, emergency and after resuscitation care corresponded to the clinical protocols “Initial, resuscitation and post-resuscitation care for newborns” protocol of the Ministry of Health of Ukraine No. 225 from 28.03.2014. and the clinical protocol “Assistance to newborns with respiratory disorders” No. 484 dated 21.08.2008.

The study was conducted in accordance with the provisions of the GCP (1996) and the Helsinki Declaration on Biomedical Research, in which humans are the subject of subsequent revisions of the Council of Europe Convention on Human Rights and Biomedicine (April 4, 1997) and the recommendations of the Bioethics Committee at the Presidium of the Academy of Medical Sciences of Ukraine (2002), as well as Orders of the Ministry of Health of Ukraine No. 690 dated 23.09.2009, No. 944 dated 14.12.2009, No. 616 dated 03.08.2012. The work was performed with a positive conclusion of the Commission on Bioethics of Higher Education Institutions of Ukraine “Bukovynian State Medical University” (minutes No. 2 dated 19.10.2017) and the local commission on biomedical ethics at the Khmelnytsky Regional Perinatal Center (minutes No. 5 dated 3.11.2017).

In particular, these ethical requirements outweighed the benefits over the risk of side effects, the informed consent of the parents of the newborn, adherence to the principles of confidentiality and respect for the child who is incapable of self-defense, and other ethical principles for the children studied.

A full range of clinical and laboratory studies, including determination of oxygen status of capillary blood. The study included 8 (47.05 %) boys and 9 (52.94 %) girls. 13 (76.47 %) of them were discharged home, 3 (17.64 %) were transferred to the department for premature newborns of the Municipal Enterprise “Khmelnytsky City Children’s Hospital”, 1 (5.8 %) child died. Infants with hemodynamically significant Botal duct and necrotizing enterocolitis who required surgical correction were excluded from the study. Table 1 shows the characteristics of infants with sepsis.

Studies of acid-base status of blood and oxygen status of capillary blood were performed on each child daily on a MEDICA Easy Stat analyzer, USA.

Analysis of capillary blood oxygen status included the following studies: pH, pO<sub>2</sub>, pCO<sub>2</sub>, HCO<sub>3</sub> (capillary blood bicarbonate concentration), BEb<sub>3</sub> (base surplus/deficiency),

Beef<sub>3</sub> (standard base surplus/deficiency), SBC (standard bicarbonate), % SO<sub>2</sub> (the amount of oxygen saturation (at normal P<sub>50</sub>) of hemoglobin of capillary blood), O<sub>2</sub>ct (oxygen content in capillary blood), AdDO<sub>2</sub> (alveolar-capillary oxygen gradient), RI (respiratory coefficient). The calculations were performed automatically by the analyzer.

The studies were performed on the first day after birth, on the third day in the intensive care unit, when the newborns were mostly on oxygen donation, and on the seventh day, which is associated with stabilization. When calculating the respiratory index (RI) instead of the parameters of PaO<sub>2</sub>, the level of pO<sub>2</sub> of capillary blood +20 mmHg was used [5]. Respiratory index was evaluated by the ratio:  $RI = pO_2 / FiO_2$ , where pO<sub>2</sub> - partial pressure of capillary blood oxygen +20 (mmHg); FiO<sub>2</sub> – inspiratory oxygen fraction (%). The degree of dysfunction of the respiratory system was studied by mechanical ventilation by inspiratory pressure (PIP) and FiO<sub>2</sub> in the inhaled mixture, which was obtained by multiplying these indicators (PIP×FiO<sub>2</sub>). This indicator allows us to simultaneously assess the degree of respiratory disorders and the need for respiratory support in premature infants with the impossibility of frequent invasive interventions. Criteria for respiratory support were assessed individually according to the clinical protocols “Initial, resuscitation and resuscitation of newborns” protocol of the Ministry of Health of Ukraine No. 225 from 28.03.2014 and Clinical protocol “Assistance to newborns with respiratory disorders” No. 484 from 21.08.2008.

The non-parametric method of statistical analysis was used for statistical calculation: U Mann-Whitney test and computer program of statistical analysis STATISTICA 6. Descriptive statistics are presented in the form of medians and percentiles.

## 5. Results

Homogeneity of the group by gestational age and birth weight allowed to exclude the influence of these indicators on the degree of maturity of the respiratory and central nervous system, the formation of bronchopulmonary dysplasia, duration of mechanical ventilation, oxygen status of capillary blood.

The main characteristics of the oxygen status of capillary blood and the calculated respiratory indices in premature infants with neonatal sepsis are given in Table 2.

Table 1

General characteristics of the examined children

No.	Indicators (N=17)	Me (25–75 %)
1	Birth weight, grams	1240 (800–1420)
2	Mother’s age, years	26 (24–26)
3	Gestation period, weeks	28 (28–32)
4	Apgar score for 1 minute, point	4 (3–5)
5	Apgar score for 5 minutes, point	5 (4–6)
6	Duration of ALV, days	6 (3–7)
7	Duration of nCPAP, days	7 (6–7)
8	The length of stay of patients in the hospital, bed – days	45 (38–64)

Table 2  
Indicators of oxygen status of capillary blood in premature infants with neonatal sepsis. Me (25–75 %)

Indicators (points)	1st day+ N=16	3rd day++ N=13	7th day+++ N=10
pH	7.30 (7.24–7.33)	7.32 (7.26–3.38)	7.38 (7.24–7.44)
pO <sub>2</sub> (mm Hg)	57 (50–66.5)	59 (48–75)	53 (41–69)
pCO <sub>2</sub> (mm Hg)	40* (35–49)	27.1 (23.4–34.8)	31.65*** (15.6–40.6)
HCO <sub>3</sub> (mmol/l)	20.6** (17.2–21.8)	17.4 (15.3–18.4)	14.45*** (11.5–21.7)
BE <sub>b</sub> (mmol/l)	–6.7 (–8.3 – –4.6)	–7.1 (–9.5 – –1.3)	–6.7 (–14.6 – –2.3)
B <sub>cef</sub> (mmol/l)	–7.1* (–9.1 – –5.2)	–4.1 (–8.3 – 11.5)	–8.4*** (–16.4 – –2.7)
SBC (mmol/l)	19.5 (17.8–20.9)	18.5 (16.5–19.3)	19.65*** (12.6–25.8)
%SO <sub>2</sub>	86.25 (82.4–94.8)	88.02 (81.3–94.9)	88.15 (77.1–94.2)
Ct O <sub>2</sub> (ml/dl)	21.40 (18.4–22.8)	20.9 (17.7–22.5)	16.5** (16.1–17.8)
AdDO <sub>2</sub> (mm Hg)	68* (42–130)	90 (56–132)	92.5*** (70–185)
RI	1 (0.7–2.76)	1.9 (0.7–2.5)	2.35*** (1.65–3.75)
RI	3.57 (2.26–3.87)	3.09 (2.19–3.95)	2.9 (2.76–3.85)
(PIP x FiO <sub>2</sub> )	7.0* (3.78–12)	3.37* (2.3–4.59)	3.25** (2.5–4.8)

Note: \* –  $P1:2 < 0.05$ ; \*\* –  $P1:3 < 0.05$ ; \*\*\* –  $P2:3 < 0.05$ ; + – one child was not taken for the first day due to the severity of the condition; ++ – for 3 days three children were without oxygen subsidy, +++ – for 7 days 6 children were without oxygen subsidy. One child died on the second day of life

## 6. Discussion

There were statistically significant changes in oxygen status depending on the day of life for pCO<sub>2</sub>, HCO<sub>3</sub>, B<sub>cef</sub>, SBC, O<sub>2</sub>ct, AdDO<sub>2</sub>, RI, PIP x FiO<sub>2</sub>. Differences for indicators pH, pO<sub>2</sub>, BE<sub>b</sub>, %SO<sub>2</sub>, PI were not found.

Despite the constant pO<sub>2</sub> values during the three days of observation, the statistical difference in HCO<sub>3</sub>, on the one hand, may indicate a deterioration in the general condition of infants, which is associated with the manifestation and increase in clinical signs of generalized infectious-inflammatory process with a simultaneous increase in partially compensated metabolic acidosis [6, 7]. These indicators were also influenced by the fact that the oxygen status of capillary blood was determined in only 10 infants who needed an oxygen subsidy due to the severity of the condition.

Changes in BE values coincide with the data of Turkish scientists Arayici S., Şimşek G. K., Canpo-

lat F. E., [7] and indicate that the BE value  $< -5$  mmol/l indicates a deterioration in patients and may be the first diagnostic indicator of the implementation of the septic process.

It is known that the content of oxygen in capillary blood depends on two components: the amount of oxygen coming from the lungs and the rate of its utilization by tissues. The decrease in this indicator on the seventh day may be due to impaired tissue utilization, which coincides with the identified metabolic disorders. In most cases, in clinical practice, various disorders of oxygenation are manifested in the form of reduced transcutaneous oxygen saturation of hemoglobin and partial tension of blood oxygen [8, 9, 11]. Our results allow us to conclude that while the above indicators do not change significantly, the trouble can be detected with indicators such as AdDO<sub>2</sub>, RI, which reflect the state of oxygenation with impaired ventilation-perfusion ratios, increased blood shunting and delivery processes and oxygen consumption at the tissue level. Similar results were also obtained by Perestoronina M. V., who was one of the few researchers to determine the oxygen status in premature infants [5]. The calculated indicator “PIP×FiO<sub>2</sub>” was less sensitive to assess changes in the lungs and did not correspond to the clinical picture of the severity of the condition of patients with sepsis, in contrast to patients with respiratory pathology according to Petrenko Yu. V. and others [5, 10].

**Study limitations.** The studies were performed in a small group of patients.

**Prospects for further research.** To date, there are no clear data on the use and interpretation of the use of capillary blood for long-term monitoring of oxygen transport disorders in premature infants with neonatal sepsis. There are no clear data on the specificity and sensitivity of capillary blood oxygen gradients in patients with neonatal sepsis of varying severity and complications. The decision of these problems will allow to substantiate probability of use of indicators of capillary blood for an assessment of weight of disturbances of transport of oxygen at such patients, reduction of term of stay on fat ventilation, and decrease in lethality.

## 6. Conclusions

Capillary blood oxygen status indicators can be used as alternative indicators of the severity of the condition in monitoring the function of premature infants.

Increases in the indicators on the seventh day AdDO<sub>2</sub> > 70 mm Hg ( $p < 0.05$ ), RI > 1 ( $p < 0.05$ ) indicate deterioration, even in the temporary absence of clinical signs in children with neonatal sepsis.

Data calculation of the indicator “PIP×FiO<sub>2</sub>” is less sensitive to assess the severity of premature infants with neonatal sepsis.

## Conflict of interest

The authors declare that they have no conflicts of interest.

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**Olena Vlasova**, PhD, Assistant, Department of Pediatrics and Pediatric Infectious Diseases, Higher State Educational Institution of Ukraine «Bukovinian State Medical University», Teatralna sq., 2, Chernivtsi, Ukraine, 58002  
E-mail: [vlasovaolena01@gmail.com](mailto:vlasovaolena01@gmail.com)

**Larysa Kolyubakina**, PhD, Associate Professor, Department of Pediatrics and Pediatric Infectious Diseases, Higher State Educational Institution of Ukraine «Bukovinian State Medical University», Teatralna sq., 2, Chernivtsi, Ukraine, 58002  
E-mail: [koliubakina.larysa@bsmu.edu.ua](mailto:koliubakina.larysa@bsmu.edu.ua)