https://doi.org/10.15360/1813-9779-2024-5-44-54

Efficacy and Safety of a Standardized CPAP Protocol in the Delivery Room in Late Preterm Infants with Infectious and Non-Infectious Lung Diseases

Eugene V. Shestak[1,2]*, Olga P. Kovtun[1], Ekaterina A. Mylarshikova[2], Yulia I. Nechaeva[2]

[1] Ural State Medical University, Ministry of Health of Russia,
3 Repin Str., 620028 Yekaterinburg, Sverdlovsk region, Russia
[2] Yekaterinburg Clinical Perinatal Center,
9 Komsomolskaya Str., 620066 Ekaterinburg, Sverdlovsk region, Russia

For citation: *Eugene V. Shestak, Olga P. Kovtun, Ekaterina A. Mylarshikova, Yulia I. Nechaeva.* Efficacy and Safety of a Standardized CPAP Protocol in the Delivery Room in Late Preterm Infants with Infectious and Non-Infectious Lung Diseases. *Obshchaya Reanimatologiya = General Reanimatology.* 2024; 20 (5): 44–54. https://doi.org/10.15360/1813-9779-2024-5-44-54 [In Russ. and Engl.]

***Correspondence to:** Eugene V. Shestak, shestakev@yandex.ru

Summary

The aim of this study was to evaluate the efficacy and safety of a standardized protocol of delivery room CPAP therapy in late preterm infants with acute neonatal respiratory failure (ARF) caused by various conditions.

Material and methods. A retrospective comparative study of the efficacy of the standardized CPAP protocol in the cohorts of late preterm infants (34–36 weeks) was conducted at the Yekaterinburg Perinatal Center. The comparison group (C, *N*=256) included infants who received CPAP therapy in the delivery room during 12 months in 2020 before the introduction of the standardized protocol. The study group (S, *N*=169) included infants treated with standardized CPAP in April-December, 2022. The following subgroups were identified in groups C and S based on the cause of ARF: transient tachypnea of the newborn (TTN; C: *N*=100; S: *N*=89), respiratory distress syndrome (RDS; C: *N*=84; S: *N*=39), and congenital infection (CI; C: *N*=54; S: *N*=37). Other causes of ARF in groups C and S were found in 18 and 4 infants, respectively.

Results. Switching to the standardized CPAP protocol reduced the duration of mechanical ventilation by an average of 24 h (*P*=0.013), the incidence of documented cerebral ischemia (CI) from 64.1% to 53.2% in all subgroups (*P*=0.022), the length of stay in the neonatal ward from 12 to 11 days (*P*=0.001), and the length of stay in the hospital from 16 to 14 days (*P*=0.001) as well as the incidence of CI in the STTN subgroup vs CTTN (38.2% vs. 61.0%, *P*=0.002). No significant differences were found in the RDS and CI subgroups. The frequency and duration of binasal CPAP and lung ventilation in the neonatal ICU did not differ between subgroups. Pneumothorax within the first 24 h occurred in one patient in group C and in two patients in group S (*P*=0.339), all of whom were diagnosed with congenital infection. No damage to the nasal passages was observed in any group.

Conclusion. The use of a standardized protocol of CPAP therapy for neonates born after 35 weeks of gestation with respiratory failure of any etiology can significantly reduce the severity and duration of illness and should be considered as a basic respiratory strategy in the delivery room when indicated.

Keywords: newborn; late preterm infants; CPAP; transient tachypnea of the newborn; neonatal respiratory distress syndrome; congenital infection

Conflict of interest. The authors declare no conflict of interest.

Introduction

Birth is characterized by a series of preparatory changes in the body, first in the fetus and then in the newborn. These changes include a decrease in the production of fetal lung fluid and activation of its reabsorption, as well as the production of sufficient surfactant to maintain surface tension in the open alveoli after the first breath [1]. Stress hormones (adrenaline, cortisol, etc.) produced by both the mother and fetus in response to natural term delivery significantly influence fluid clearance from the lungs [2, 3].

However, delivery at late preterm gestation age ($34^{0/7}$–$36^{6/7}$ weeks), especially via cesarean section, disrupts the neonatal adaptation to extrauterine life, which may manifest as acute respiratory failure immediately after birth or during the first hours of life [4]. Transient tachypnea of the newborn (TTN) [5, 6] and surfactant deficiency can lead to respiratory distress syndrome (RDS) [5, 7], which is associated with fetal fluid retention in the lungs. Most neonatal conditions are characterized by nonspecific acute respiratory failure (ARF), which is also observed in congenital infection (CI) [7–9]. When ARF develops in the delivery room, differentiating between TTN, RDS, and CI is extremely difficult [5]. Not only are the signs and symptoms of these conditions similar, but the morphologic changes in the lungs are as well. One study showed that hyaline membranes were found in the lungs of 93.5% of neonates with an average gestational age (GA) of 28.9±5.3 weeks, a birth weight of 1404±945 g, and a median life expectancy of 72 hours [10]. The causes of hyaline membranes were varied and included true surfactant deficiency, pneumonia, asphyxia, aspiration, shock, hemorrhagic syndrome, and others. Regardless of the etiology of ARF, the infant requires prompt and appropriate respiratory therapy. In particular, sepsis and acute respiratory distress syndrome are the

leading causes of multiorgan failure and mortality in neonates [11]. The primary method of respiratory support for neonates of any gestational age with moderate ARF is continuous positive airway pressure (CPAP) therapy [12–14].

Russian guidelines, such as the Methodological Letter of the Ministry of Health of the Russian Federation on Resuscitation and Stabilization of Neonates in the Delivery Room (2020) [15] and the National Guidelines for Neonatology (2019) [16], recommend CPAP therapy for children older than 32 weeks of gestation when ARF develops, but do not specify the criteria for initiating therapy, its continuation, efficacy, or the technique itself, including the required parameters of respiratory support. In our previous studies, we analyzed the severity of TTN in full-term neonates and the type of respiratory support used [17]. Based on these data, we developed a standardized protocol for CPAP therapy in the delivery room.

In a subsequent prospective study, the protocol was found to be highly effective in reducing the severity, duration, and incidence of brain ischemia (BI) in TTN [18].

The aim of this study was to evaluate the efficacy and safety of a standardized protocol for delivery room CPAP therapy in late preterm neonates with acute respiratory failure caused by various conditions.

Material and Methods

A single-center, retrospective cohort study was conducted on late preterm neonates ($34^{0/7}$–$36^{6/7}$ weeks of gestation) born at the Yekaterinburg Clinical Perinatal Center (YCPC) who underwent CPAP therapy in the delivery room.

The standardized protocol for CPAP therapy in preterm neonates with TTN was approved by the local ethics committee of the YCPC (Protocol No. 2 dated July 2, 2021). The protocol for CPAP therapy in the delivery room for ARF in late preterm and term neonates was implemented at the YCPC on March 11, 2022 (Decision No. 147). Parents of all neonates signed an informed consent for diagnosis and therapy, including the use of data obtained for scientific purposes.

The control group (C, *N*=256) included children treated in 2020, before the implementation of the protocol. The study group (S, *N*=169) included children hospitalized from April to December 2022, after the implementation of the protocol.

Inclusion and exclusion criteria were the same for groups C and S.

Inclusion criteria:

— Late preterm birth (GA $34^{0/7}$–$36^{6/7}$ weeks);

— Development of ARF within the first 60 minutes after birth;

— CPAP therapy in the delivery room.

Exclusion criteria:

— congenital malformations presenting with ARF;

— chromosomal abnormalities;

— any other condition that could influence the results of the study.

In groups C and S, subgroups of patients were identified according to the cause of respiratory disorders in the delivery room: for T_{TN}, the subgroups C_{TTN} (*N*=100) and S_{TTN} (*N*=89); for RDS, the subgroups C_{RDS} (*N*=84) and S_{RDS} (*N*=39); for CI, the subgroups C_{CI} (*N*=54) and S_{CI}(*N*=37).

In addition to T_{TN}, RDS, and CI, the following causes of ARF in the delivery room were identified in the control group: moderate to severe birth asphyxia (*N*=10), polycythemia (*N*=3), anemia (*N*=3), and interventricular septal defect (*N*=2).

In addition to T_{TN}, RDS and CI, the causes of ARF in the study included moderate to severe birth asphyxia (*N*=4).

All other causes of ARF in the delivery room in groups C and S were documented in infants at 34 weeks' gestation.

Inclusion and exclusion criteria were consistent between control and study subgroups (C_{TTN} and S_{TTN}, C_{RDS} and S_{RDS}; C_{CI} and S_{CI}).

Inclusion criteria:

- for the TTN subgroup, a diagnosis of TTN;
- for the RDS subgroup, a diagnosis of RDS;
- for the CI subgroup, a diagnosis of congenital infection.

Exclusion criteria: none.

The flowchart of group and subgroup recruitment is shown in Fig. 1.

Description of medical intervention. Standardized protocol for delivery room CPAP therapy. The use of a standardized protocol for delivery room CPAP therapy was first studied and described in a cohort of preterm infants with TTN [18] and subsequently in those with congenital infection [19]. The protocol was developed based on the analysis of respiratory therapy in this population [17] and the prognosis of the disease [20].

CPAP equipment and methodology. We used conventional equipment and supplies available in all delivery and operating rooms of the perinatal center. When indications were present (described below), CPAP was initiated with mask-based CPAP, followed by a transition to mononasal CPAP (hereafter referred to as CPAP) for 5 minutes. This was delivered via an endotracheal tube (ETT) inserted into the child's nasal passage to a depth equal to the midpoint of the distance between the earlobe and the nasal ala (corresponding to the level of the nasopharynx). The transition from mask-based CPAP to mononasal CPAP was prompted by the need to free the clinician's hands for further assistance to the patient. CPAP was delivered using a T-shaped resuscitation breathing circuit (Fisher &

Paykel Healthcare Limited, New Zealand), respiratory therapy devices integrated into open resuscitation stations (ORS), such as the Giraffe Warmer (General Electric, USA), BLR-2100 (MEDICOR, Hungary), or a separate device capable of titrating oxygen fraction and monitoring airway pressure, such as the Neopuff™ (Fisher & Paykel Healthcare Limited, New Zealand). Within 5 minutes of starting CPAP, the clinician placed an orogastric tube in the child and left it open. If indicated, ventilation was performed with a face mask, with transition to tracheal intubation and invasive ventilation as needed. Starting ventilation parameters were PiP 20 cm H_2O, PEEP 5 cm H_2O, FiO_2 0.21, and a rate of 40–60/min.

During the transfer of the patient from the delivery room to the NICU, the mode and parameters of respiratory support were not changed. Binasal CPAP parameters in the NICU were 4–8 cm H_2O, with an initial FiO_2 of 0.21. The respiratory support device used during transport of the infant to the NICU for CPAP or ventilation was the Stephan Reanimator F120 (Stephan GmbH, Germany) with a breathing circuit (Kometaline, Russia). Respiratory support devices for CPR in the NICU included the Infant Flow CPR (VIASYS Healthcare Inc., USA) and the Infant Flow circuit with a set of consumables (humidifier chamber, cap, nasal cannulae) (Vincent Medical, China). Respiratory support devices for NICU ventilation included the Avea (VIASYS Healthcare Inc., USA) and the SLE-5000 (SLE Limited, UK). CPAP equipment and technique did not differ between groups C and S.

CPAP parameters. The initial mean airway pressure (MAP) was set at 8 cm H_2O with an oxygen fraction (FiO_2) of 21%. The oxygen concentration could be gradually increased or decreased to maintain the saturation (SpO_2) on the right arm in the range of 91–95%. CPAP parameters and indications for its initiation in the groups are listed in Table 1.

Indications for initiation of CPAP therapy and routing of patients in the delivery room according to the protocol. CPAP was initiated according to the protocol when the neonate developed ARF with Downes score ⩾3 points.

After 20 minutes of CPAP, the Downes score of ARF was assessed:

- if the score was <3 points, the endotracheal tube was removed from the nose and the child was monitored by the physician for 5 minutes:
- if the ARF score remained <3 during this period and no other organ or system dysfunction was observed, the infant was transferred to the neonatal unit (NNU);
- if the ARF score increased to 3 or higher, the clinician resumed CPAP using the MAP and FiO_2 parameters described above;
- CPAP was continued without changing the initial parameters if the ARF score remained at the baseline level of 3–5 points;
- if the ARF score increased from 3–4 to 5 or more points, or from 5 to 6 or more points, the infant was transferred to the NICU with the appropriate type of respiratory support (CPAP or ventilation);
- if the ARF score remained at the baseline level of 6 points or increased, the infant was transferred to the NICU with the appropriate type of respiratory support (CPAP or ventilation).

Similar actions were performed 40 and 60 minutes after CPAP initiation. At the same time, the infant was transferred to the NICU if the Downes score at

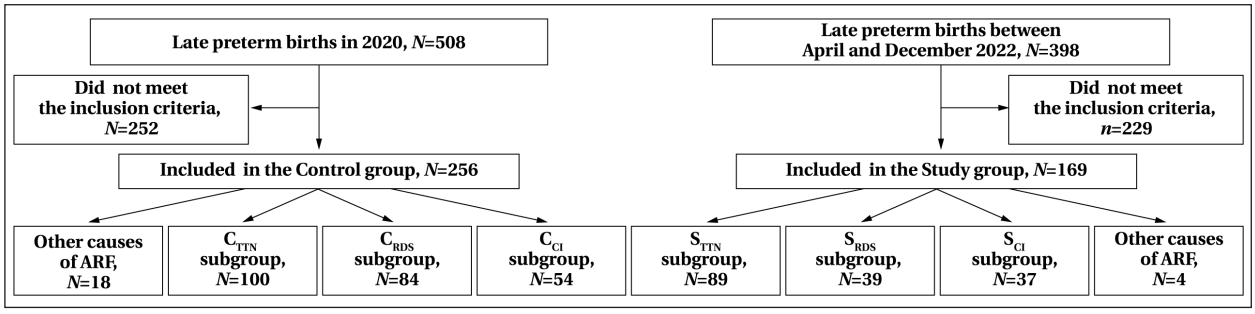

Fig. 1. Study flowchart.
Note. C — control group; S — study group; TTN — transient tachypnea of newborns; RDS — respiratory distress syndrome; CI — congenital infection.

Table 1. CPAP parameters and indications for CPAP in the delivery room.

Criterion	Control group	Study group
Interface	Face mask with switch to nasal mask CPAP	
CPAP therapy when Downes score ⩾4 points	Always	
CPAP therapy when Downes score = 3 points	At doctor's discretion	Always
CPAP therapy when Downes score = 2 points	At doctor's discretion	Never
MAP, cm H_2O	5–10	8
FiO_2, %	21	
Duration of CPAP, min	5–30	20–60
Orogastric tube placement within 5 minutes after CPAP initiation	Always	

Note. MAP — mean airway pressure; FiO_2 — fraction of inhaled oxygen; CPAP — continuous positive airway pressure

60 minutes remained the same (3–5 points at 40 minutes) or increased (Fig. 2). Neonates were transferred from the neonatal unit (NNU) and NICU to the neonatal pathology unit (NPU) if they required additional treatment and monitoring.

Study Outcomes.

— Frequency of brain injury (brain ischemia and IVH)

— Frequency and duration of mechanical ventilation

— Frequency and duration of NICU admission

— Total length of hospital stay

Methods of outcome assessment. Study outcomes were determined by analyzing data from primary medical records, such as the neonate's medical chart.

CPAP therapy safety parameters:

— Air leak syndrome diagnosed by radiological examination within the first 24 hours after birth

— Damage to the nasal passages (swelling, bleeding) diagnosed by clinical examination.

All study parameters were recorded throughout the hospital stay at the participating medical center.

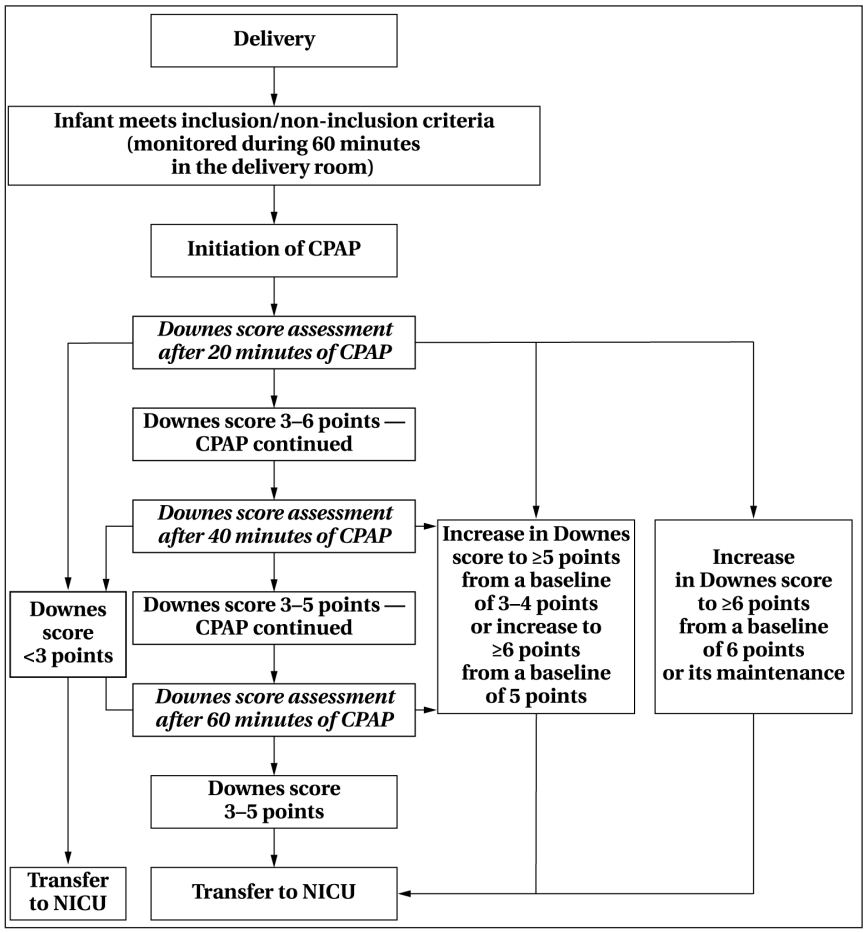

Fig. 2. Routing of neonates during CPAP therapy in the delivery room according to protocol (study group)

Note. CPAP — continuous positive airway pressure; NICU — neonatal intensive care unit; NNU — neonatal unit.

Diagnostic criteria:

— The diagnosis of TTN was made when other causes of ARF were excluded.

— The diagnosis of RDS was made on the basis of characteristic ground-glass opacities in the lungs and the absence of clinical and laboratory evidence of infection

— Congenital infection was defined by manifestations of infection within the first 72 hours after birth; the exact diagnoses were made based on the standard definition of cases according to the local YCPC protocol: early neonatal sepsis (ICD-10 P36), congenital pneumonia (ICD-10 P23), infection specific to the perinatal period (ISPP) (ICD-10 P39). The diagnosis of infection was made both with and without a positive bacterial culture from the site of infection, based on a combination of clinical, instrumental, and laboratory data

— Prolonged time between rupture of membranes and delivery was defined as amniorrhea occurring more than 18 hours before delivery

— The diagnosis of BI was made based on clinical presentation, neurosonography, and a report from a pediatric neurologist; the severity of BI was classified according to the Classification of Perinatal Neural System Lesions in Newborns (ICD-10 P91.0).

Principles of sample size calculation. Sample size was not calculated in advance. A continuous sampling design was employed.

Methods of statistical analysis. Accumulation, correction, systematization of the initial information, and visualization of the obtained results were performed using Microsoft Office Excel 2016. Statistical analysis was conducted with IBM SPSS Statistics v.27 (IBM Corporation) and BioStat (AnalystSoft Inc.) software. The normality of the distribution of quantitative parameters was assessed using the Shapiro–Wilk test (for samples with fewer than 50 values) or the Kolmogorov-Smirnov test (for samples with 50 or more values). Non-normally distributed variables were described by the median *(Me)* and lower and upper quartiles *(LQ; UQ)*. Nominal data were represented as absolute values and percentages. The Mann–Whitney *U*-test was used to compare quantitative data in independent groups, while Pearson's χ^2 test was applied for qualitative variables. When the frequency of a parameter was

less than 10, the χ^2 test with Yates' correction was used. The arithmetic mean *(M)*, standard deviation *(SD)*, and Student's *t*-test were utilized to describe numerical parameters with a normal distribution. Differences were considered significant at $P<0.05$; a two-sided *P* level of significance was applied.

Results and Discussion

When analyzing the general characteristics of the neonates, we found that GA and Apgar scores at 1 and 5 minutes were comparable in groups C and S (Table 2). There were significantly fewer boys in group C, and patients in this group were characterized by lower birth weight.

There were no significant differences in birth weight, sex, GA, and Apgar scores at 1 and 5 minutes ($P>0.05$) among the compared subgroups of patients with TTN, RDS, and CI.

Comparative analysis of the incidence of brain injury showed that children in the control group were diagnosed with brain injury significantly more often overall; however, there was no significant difference in the incidence of mild-to-moderate and severe brain injury. The frequency of IVH did not differ significantly between groups, including IVH grades 1–2 and 3–4: 1 case was recorded in the control group and none in the study group (Table 3).

Comparative analysis of respiratory therapy (Table 4) in the patient groups showed that CPAP therapy in the delivery room was significantly longer in group C, in accordance with the implemented protocol. Surfactant was administered to a comparable number of patients in both groups. The frequency of binasal CPAP (BinCPAP) in the NICU and its duration did not differ between groups. Lung ventilation in the NICU was performed in a similar number of patients in both groups, but it was significantly longer in group C. The frequency of hospitalization in the NPU and NICU, as well as the duration of hospitalization in the NICU, did not differ between the groups; however, the duration of stay in the NPU and the total length of hospitalization were significantly shorter in group S. One case of pneumothorax was recorded in group C

Table 2. Patient characteristics in groups, *Me (LQ; UQ)*, *N* (%).

Parameter	Values in groups		*P*-value
	Group C, *N*=256	Group S, *N*=169	
Gestational age, weeks	35 (34; 36) *Me*=34.792 *SD*=±0.826	35 (34; 36) *Me*=34.9 *SD*=±0.803	0.063 *t*-test (0.058)
Male sex	116 (45.3)	97 (57.4)	0.015*
Birth weight, grams	2310 (2035; 2640)	2480 (2140; 2780)	0.019*
Apgar score at 1 minute, points	6 (6; 7)	6 (6; 7)	0.395
Apgar score at 5 minute, points	7 (7; 8)	7 (7; 8)	0.919

Note. * — significant difference between groups.

Table 3. Comparison of the incidence of brain injury in patients, number (%)

Parameter	Values in groups		*P*-value
	Group C, *N*=256	Group S, *N*=169	
BI, total	164 (64.1)	90 (53.2)	0.022*
BI, mild and moderate severity	157 (95.7)	89 (98.8)	0.169
BI, severe	7 (4.3)	1 (1.2)	
IVH, total	60 (23.4)	33 (19.5)	0.340
IVH, grade 1–2	59 (98.3)	33 (100.0)	0.456
IVH, grade 3–4	1 (1.7)	0 (0)	

Note. * — significant difference between groups. For Tables 3, 5, 6, 8: BI — brain ischemia; IVH — intraventricular hemorrhage.

Table 4. Respiratory therapy and hospital stay in the groups of patients, *Me (LQ; UQ)*, *N* (%).

Parameter	Values in groups		*P*-value
	Group C, *N*=256	Group S, *N*=169	
Duration of CPAP in the delivery room, min	15 (10; 15)	40 (20; 40)	<0.001*
Administration of surfactant	40 (15.6)	21 (12.4)	0.357
BinCPAP in NICU	177 (69.1)	120 (71.0)	0.682
Duration of BinCPAP, days	1 (1; 1)	1 (1; 1)	0.222
Lung ventilation in NICU	40 (15.6)	24 (14.2)	0.688
Duration of ventilation, days	3 (1; 5)	2 (1; 3)	0.013*
Admitted to NICU	180 (70.3)	120 (71.0)	0.878
Duration of NICU stay, days	1 (1; 3)	1 (1; 2)	0.217
Admitted to NPU	242 (94.5)	154 (91.1)	0.173
Duration of NPU stay, days	12 (10; 18)	11 (9; 14)	0.001*
Total length of hospital stay, days	16 (12; 21)	14 (11; 18)	0.001*
Pneumothorax within the first 24 hours	1 (0.3)	2 (1.1)	0.339
Death	2 (0.7)	0 (0.0)	0.250

Note. * — significant difference between groups. For Tables. 4, 5, 6, 8: CPAP — continuous positive airway pressure; BinCPAP — binasal CPAP; NICU — neonatal intensive care unit, NPU — neonatal pathology unit.

compared to two cases in group S. One case of pneumothorax during the first 24 hours after birth was observed in each subgroup, as well as two deaths in subgroup C.

Subgroup analysis of patients with TTN. Analysis of the incidence of brain injury showed that mild and moderate BI were diagnosed more frequently in the C_{TTN} subgroup, and no statistically significant difference was found in the incidence of grade 1–2 IVH between the compared subgroups. No severe BI or grade 3–4 IVH was observed in either subgroup (Table 5).

CPAP therapy in the delivery room was statistically longer in the S_{TTN} subgroup. There were no significant differences between subgroups in the frequency and duration of BinCPAP use in the NICU, or in the frequency and duration of ventilation (Table 6).

There were no significant differences between subgroups in the frequency of NICU admission, NPU admission, or NICU length of stay. Length of stay in the NPU and total length of stay in the perinatal center were significantly lower in the S_{TTN} subgroup.

Only one neonate with TTN was identified at $34^{0/7}$–$34^{6/7}$ weeks of gestation in the S_{TTN} subgroup, and there were no neonates with TTN and CPAP in the delivery room in the C_{TTN} subgroup at this gestational age.

Subgroup analysis of patients with RDS. Analysis of the frequency of detection of brain injury showed no differences in the overall frequency of

Table 5. Comparison of incidence of brain injury, respiratory therapy parameters, and hospitalization characteristics of patients in the TTN subgroup, *Me (LQ; UQ)*, number (%).

Parameter	Values in groups		*P*-value
	C_{TTN}, *N*=100	S_{TTN}, *N*=89	
BI, total	61 (61.0)	34 (38.2)	0.002*
BI, mild and moderate severity	61 (100)	34 (100)	
BI, severe	0 (0)	0 (0)	
IVH, total	18 (18.0)	15 (16.9)	0.836
IVH, grade 1–2	18 (100)	15 (100)	
IVH, grade 3–4	0 (0)	0 (0)	
Duration of CPAP in the delivery room, min	15 (15; 20)	40 (20; 40)	<0.001*
BinCPAP in NICU, *N*	57 (57.0)	47 (52.8)	0.563
Duration of BinCPAP, days	1 (1; 1)	1 (1; 1)	0.976
Lung ventilation in NICU, *N*	1 (1.0)	2 (2.2)	0.493
Duration of lung ventilation, days	1 (1; 1)	1 (1; 1)	1.0
Admitted to NICU, *N*	58 (58.0)	47 (52.8)	0.473
Duration of NICU stay, days	1 (1; 1)	1 (1; 1)	0.725
Admitted to NPU, *N*	91 (91.0)	75 (84.3)	0.158
Duration of NPU stay, days	10 (8; 13)	9 (7; 12)	0.022*
Total length of hospital stay, days	13 (11; 15)	12 (9; 14)	0.018*

Note. * — significant difference between groups.

Table 6. Comparison of incidence of brain injury, respiratory therapy parameters, and hospitalization characteristics of patients in the RDS subgroup, *Me (QL; QU), N* (%).

Parameter	Values in groups		*P*-value
	C_{RDS}, *N*=8	$И_{RDS}$, *N*=39	
BI, total	57 (67.9)	28 (71.8)	0.660
BI, mild and moderate severity	54 (94.7)	7 (96.4)	0.843#
BI, severe	3 (5.3)	1 (3.6)	
IVH, total	24 (28.6)	8 (20.5)	0.343
IVH, grade 1–2	24 (100)	8 (100)	
IVH, grade 3–4	0 (0)	0 (0)	
Duration of CPAP in the delivery room, min	15 (12,5; 15)	20 (20; 40)	<0.001*
Intubated in the delivery room	1 (1.2)	0	0.494
Administration of surfactant	21 (25.0)	10 (25.6)	0.939
Surfactant using the INSURE technique	20 (23.8)	10 (25.6)	0.826
Surfactant through the endotracheal tube	1 (1.2)	0	0.494
Surfactant 1 time	20 (23.8)	9 (23.1)	0.929
Surfactant 2 times	1 (1.2)	1 (2.6)	0.575
BinCPAP in NICU, n	68 (81.0)	39 (100)	0.003*
Duration of BinCPAP, days	1 (1; 1)	1 (1; 1)	0.302
Lung ventilation in NICU, n	2 (2.4)	2 (5.1)	0.424
Duration of lung ventilation, days	2 (1; 3)	1 (1; 1)	0.617
Admitted to NICU, n	69 (82.1)	39 (100)	0.005*
Duration of NICU stay, days	1 (1; 1)	1 (1; 1)	0.171
Admitted to NPU, n	84 (100)	39 (100)	1.0
Duration of NPU stay, days	15 (12; 22)	16 (12; 23)	0.662
Total length of hospital stay, days	19 (14.5; 25)	20 (16; 25)	0.342

Note. # — Chi-square test with Yates correction. * — significant difference between subgroups. For Tables 6, 8: INSURE — surfactant administration technique including tracheal intubation, surfactant administration, tracheal extubation.

brain injury, including mild, moderate, and severe BI, among the subgroups. No significant differences were found in the incidence of grade 1–2 IVH. No grade 3–4 hemorrhage was observed in any of the subgroups (Table 6). Comparative analysis of respiratory therapy parameters showed that the duration of CPAP in the delivery room was significantly shorter in the C_{RDS} subgroup; the frequency of BinCPAP use in the NICU was lower in the C_{RDS} subgroup, with the same median duration of 1 day, and the frequency of ventilation and its duration were comparable between the subgroups. Only 1 infant in the C_{RDS} subgroup was intubated in the delivery room. Surfactant was administered in 25% of patients in both subgroups. Analysis of the methods and frequency of surfactant administration showed no statistically significant differences. The frequency of NICU admission was higher in the S_{RDS} subgroup, with the same median NICU length of stay of 1 day. All patients in both subgroups were treated in the NICU with a comparable length of stay, while the total length of stay in the perinatal center was 19 (14.5; 25) days in the C_{RDS} subgroup and 20 (16; 25) days in the S_{RDS} subgroup, with no statistically significant difference. Eighty-two (97.6%) infants in the C_{RDS} subgroup and all 39 (100%) infants in the S_{RDS} subgroup were enrolled during week $34^{0/7}$–$34^{6/7}$ of GA.

Subgroup analysis of patients with CI. No statistically significant subgroup differences were found in the incidence of congenital pneumonia, early neonatal sepsis, and infections specific to the perinatal period (Table 7).

The frequency of CI was comparable in the subgroups, including mild, moderate, and severe. Twenty-five percent of patients in both subgroups had IVH, including grade 1–2 IVH. Only one case of grade 3–4 IVH was observed in the C_{CI} subgroup (Table 8).

CPAP duration was significantly shorter in the C_{CI} subgroup; the frequency of BinCPAP use in the NICU and its duration did not differ. Surfactant was administered to a similar number of patients in both subgroups. The percentage of patients receiving mechanical ventilation did not differ, but the duration of mechanical ventilation was significantly longer in the C_{CI} subgroup (Table 9). The frequency of admission to the NICU did not differ between the subgroups, but the duration of treatment for children in the NICU was longer in the C_{CI} subgroup. A similar number of patients were admitted to the NPU in both subgroups, though the hospital stay was longer in the C_{CI} subgroup, without a statistically significant difference.

Two deaths were documented in the C_{CI} subgroup (*P*=0.241). The hospital stay was significantly longer in this subgroup.

Adverse events. Pneumothorax during the first 24 hours occurred in one patient in the control group and in two patients in the study group (*P*=0.339); all 3 patients were diagnosed with infection. No damage to the nasal passages was observed in the studied groups.

Table 7. Diagnoses in patients of CI subgroups, *Me (LQ; UQ), N* (%)

Parameter	Values in groups		*P*-value
	C_{CI}, *N*=54	S_{CI}, *N*=37	
Congenital pneumonia	23 (42.5)	17 (45.9)	0.752
Early neonatal sepsis	17 (31.4)	9 (24.3)	0.458
Infection specific for the perinatal period	14 (25.9)	11 (29.7)	0.690

Table 8. Comparison of incidence of brain injury, respiratory therapy parameters, and hospitalization characteristics of patients in the CI subgroup, *Me (LQ; UQ)*, number (%).

Parameter	Values in groups		*P*-value
	C_{CI}, *N*=54	S_{CI}, *N*=37	
BI *(N)*, of them:	34 (62.9)	26 (70.2)	0.471
BI, mild and moderate severity *(N)*	30 (88.2)	26 (100)	0.198
BI, severe *(N)*	4 (11.8)	0 (0)	
IVH *(N)*, of them:	14 (25.9)	9 (24.3)	0.863
IVH, grade 1–2 *(N)*	13 (92.8)	9 (100)	0.820
IVH, grade 3–4 *(N)*	1 (7.2)	0 (0)	
Duration of CPAP in the delivery room, min	15 (10; 15)	40 (20; 40)	<0.001*
Administration of surfactant, *N*	19 (35.1)	11 (29.7)	0.587
BinCPAP in NICU, *N*	52 (96.2)	34 (91.8)	0.366
Duration of BinCPAP, days	2 (1; 3)	1 (1; 2)	0.064
Lung ventilation in NICU, *N*	37 (68.5)	20 (54.0)	0.162
Duration of lung ventilation, days	3 (2; 5)	2 (1; 3)	0.032*
Admitted to NICU, *N*	53 (98.1)	34 (91.8)	0.153
Duration of NICU stay, days	5 (3; 7)	3 (2; 6)	0.024*
Admitted to NPU, *N*	49 (90.7)	36 (97.2)	0.216
Duration of NPU stay, days	14 (10; 18)	11 (9; 14.5)	0.075
Death, *N*	2 (3.7)	0	0.241
Total length of hospital stay, days	19,5 (16; 23)	16 (13; 19)	0.037*

Note. * — significant difference between subgroups.

Discussion

BI was diagnosed less frequently in the study group than in the control group, 53.2% vs. 64.1% (*P*=0.022). However, a significant difference in BI was found only in patients with TTN, 38.2% vs. 61.0% (*P*=0.002). After the implementation of a standardized protocol for CPAP therapy in the routine work of the perinatal center, the frequency of CPAP use in the delivery room significantly decreased in this cohort of children (*P*=0.018). In the group of premature neonates who received CPAP therapy according to the protocol, positive results were observed regarding the severity and duration of the diseases that caused ARF, namely a decrease in the frequency of BI and the total length of hospital stay from 16 to 14 days (*P*=0.049).

Treatment of patients with TTN according to the CPAP therapy protocol had a significant effect on their clinical status: the duration of mechanical ventilation was reduced by an average of 1 day (*P*=0.013), the frequency of BI was reduced from 64.1% to 53.2% (*P*=0.022), the length of stay in the NPU decreased from 12 to 11 days (*P*=0.001), and the total length of hospital stay was reduced from 16 to 14 days (*P*=0.001).

In the group of patients with RDS, the CPAP protocol was not effective but was associated with an increase in the frequency of NICU admission from 82.1% to 100% of patients (*P*=0.005).

In patients with CI, the use of the protocol resulted in a decrease in severity and duration of illness: a decrease in duration of mechanical ventilation from 3 to 2 days (*P*=0.032), a decrease in duration of NICU stay from 5 to 3 days (*P*=0.024), and a decrease in total hospital stay from 19.5 to 16 days (*P*=0.037).

Analysis of diagnoses and GA showed that at $34^{0/7}$–$34^{6/7}$ weeks, 121 (98.3%) out of 123 infants with RDS were enrolled in the control and study groups, and only 1 (0.5%) infant with TTN out of 189 patients in the control and study groups. In contrast, patients with CI were observed at all gestational ages, but their numbers were significantly lower compared to those with TTN and RDS. A large national multicenter study showed that 80–100% of neonates admitted to the NICU at $34^{0/7}$–$36^{6/7}$ weeks' gestation required respiratory support, and the most common cause of ARF in this study was RDS [21]. The median GA in this study was 34.0 (34.0; 35.0) weeks, which correlates with our findings.

Due to the proven efficacy of the CPAP protocol in patients with TTN and the lack of a positive effect in patients with RDS, we decided to change the protocol indications for CPAP therapy, specifically by increasing the minimum GA to $35^{0/7}$ weeks.

Comparison of the control and study groups showed that the main causes of ARF in the delivery room in late preterm neonates with GA of $35^{0/7}$–$36^{6/7}$ weeks (*N*=247) were:

— TTN (*N*=188; 76.1%);
— CI (*N*=57; 23.1%);
— RDS (*N*=2; 0.8%).

According to previous studies, the incidence of TTN increases with decreasing GA at birth: 0.2–0.6% in preterm neonates [22, 23], 5% in neonates at GA 35–36 weeks, and up to 10% in neonates at 33–34 weeks gestation [24–26]. Intrauterine fetal infection is the most established factor for premature rupture of membranes and preterm birth [27, 28], and stillbirths due to congenital infection can be as high as 10–25%, even in countries with high socioeconomic levels [29–31]. The concept of early neonatal infection is typically defined by the onset of symptoms in the first 72 hours after birth [32]. In the delivery room, when the primary respiratory disorder develops, the differential diagnosis of TTN and CI is challenging. The clinical presentation of ARF in newborns is not specific, and both conditions do not have characteristic symptoms. Laboratory diagnosis of CI in the delivery room is limited due to the absence of changes in complete blood count and inflammatory markers (C-reactive protein and procalcitonin) in most cases in the first hours after birth, and radiologic examination is cumbersome [6, 7, 32]. The need for immediate care of the infant prompted us to conduct several studies to develop and evaluate the efficacy of a standardized respiratory therapy protocol, regardless of the primary condition, based solely on the assessment of ARF. Taking into account the above data, the developed protocol for CPAP therapy can be considered as a universal method for the treatment of ARF in the delivery room for preterm and premature infants from 35 weeks of gestation, provided the protocol criteria are met.

Brain ischemia resulting from respiratory disorders and hypoxemia has been described as a consequence of RDS and infection [33], but no studies have been found to suggest an association between brain damage and TTN in late preterm infants.

Our previous studies on TTN in preterm infants have shown an association of this condition with functional and biochemical changes in the brain, characterized by a low level of cerebral oxygenation after birth and its gradual increase [34], as well as lower levels of nerve growth factor beta (NGF-β) 6–12 hours after birth compared to healthy preterm infants [35]. Furthermore, the use of a standardized protocol of CPAP therapy in the delivery room in preterm infants with TTN reduced the incidence of BI (from 85.5% to 29.1%, *P*=0.001), the incidence of infant admission to the NICU (from 70.3% to 18.2%, *P*=0.001), and the total length of hospital stay (from 10 (7; 12) to 3 (2; 7) days, *P*=0.001) [16]. On the other hand, the use of the same CPAP protocol in preterm infants with infections did not affect the

incidence of the above outcomes but also did not worsen their condition [19].

Considering that TTN is the most common cause of ARF in the delivery room in neonates born over $35^{0/7}$ weeks of gestation, and that TTN and CI together account for 95–99% of ARF cases, the application of the CPAP protocol in late preterm neonates at GA over $35^{0/7}$ weeks with ARF of any etiology is justified from both a scientific and practical perspective as a standardized method that significantly reduces the severity of the disease and the duration of treatment.

Study limitations:

1. Single-center, retrospective nature of the study.

2. Significant differences in baseline characteristics of the control and study groups regarding sex and birth weight, which may have a confounding effect.

Conclusion

The developed standardized protocol of CPAP therapy in the delivery room has demonstrated high efficacy and safety and can be recommended as a basic method of therapy for late preterm neonates. The maximum efficacy of the protocol was achieved in patients with TTN, which is the predominant cause of ARF in this cohort.

References

1. *Hooper S. B., Te Pas A. B., Kitchen M. J.* Respiratory transition in the newborn: a three-phase process. *Arch Dis Child. Fetal Neonatal Ed.* 2016; 101 (3): F266–271. DOI 10.1136/archdischild-2013-305704. PMID: 26542877.
2. *Brown M. J., Olver R. E., Ramsden C. A., Strang L. B., Walters D. V.* Effects of adrenaline and of spontaneous labour on the secretion and absorption of lung liquid in the fetal lamb. *J Physiol.* 1983; 344: 137–152. DOI 10.1113/jphysiol.1983.sp014929. PMID: 6655575.
3. *Umran R. M. R., Khalil R. M.* Association between low cord serum cortisol level and transient tachypnea of the newborn in late preterm and term neonates delivered by elective cesarean section. *Am J Perinatol.* 2022; 39 (11): 1254–1260. DOI: 10.1055/s-0040-1722603. PMID: 33454947.
4. *Mahoney A. D., Jain L.* Respiratory disorders in moderately preterm, late preterm, and early term infants *Clin Perinatol.* 2013; 40 (4): 665–678. DOI 10.1016/j.clp.2013.07.004. PMID: 24182954.
5. *Овсянников Д. Ю., Бойцова Е. В., Жесткова М. А., Кршеминская И. В., Ашерова И. К., Украинцев С. Е., Межинский С. С.* Неонатальная пульмонология: Монография. (ред. Овсянников Д. Ю.). М.: Севен-Принт; 2022: 168. *Ovsyannikov D. Yu., Boitsova E. V., Zhestkova M. A., Krsheminskaya I. V., Asherova I. K., Ukraintsev S. E., Mezhinsky S. S.* Neonatal pulmonology: Monograph. (ed. Ovsyannikov D. Yu.). M.: Seven-Print; 2022: 168. (in Russ.). ISBN 978-5-91556-757-2. EDN NGFFJV.
6. *Шестак Е. В., Ковтун О. П., Ксенофонтова О. Л.* Транзиторное тахипноэ у новорожденных: монография; ред. Ковтун О. П. д-р мед. наук, проф., акад. РАН; М-во здравоохранения РФ, Урал. гос. мед. ун-т. Екатеринбург : УГМУ; 2023: 144. *Shestak E. V., Kovtun O. P., Ksenofontova O. L.* Transient tachypnea in newborns: monograph; ed. Kovtun O. P. Doctor of Medical Sciences, Professor, acad. RAS; Ministry of Health of the Russian Federation, Ural State Medical University Yekaterinburg: USMU; 2023: 144. (in Russ.). ISBN 978-5-00168-047-5.
7. *Овсянников Д. Ю., Володин Н. Н.* Заболевания легких новорожденных: трудности диагностики, диагностические критерии и последствия. *Педиатрия. Журнал им. Г. Н. Сперанского.* 2022; 101 (3): 170–177. *Ovsyannikov D. Yu., Volodin N. N.* Lung diseases in newborns: diagnostic difficulties, diagnostic criteria and consequences. *Pediatrics. G.N Speransky J. = Pediatria. Zhournal im. G. N. Speranskogo*. 2022; 101 (3): 170–177. (in Russ.). DOI: 10.24110/0031-403X-2022-101-3-170-177.
8. *Антонов А. Г., Байбарина Е. Н., Балашова Е. Н., Дегтярев Д. Н., Зубков В. В., Иванов Д. О., Ионов О. В., с соавт.* Врожденная пневмония: клинические рекомендации. *Неонатология: новости, мнения, обучение.* 2017; 4: 133–148. *Antonov A. G., Baibarina E. N., Balashova E. N., Degtyarev D. N., Zubkov V. V., Ivanov D. O., Ionov O. V., et al.* Congenital pneumonia: clinical recommendations. *Neonatology: News, Opinions, Training = Neonatologiya: Novosti, Mneniya, Obucheniye.* 2017; 4: 133–148. (in Russ.). DOI 10.24411/2308-2402-2017-00049.
9. *Шестак Е. В.* Кистозно-аденоматозная мальформация легкого II типа у новорожденного, проблемы ранней диагностики. *Уральский медицинский журнал.* 2022; 21 (1): 77–84. *Shestak E. V.* Cystic adenomatous lung malformation of type II in the newborn, problems of early diagnosis. *Ural Medical Journal = Uralskiy Meditsinskiy Zhurnal.* 2022; 21 (1): 77–84. (in Russ.). DOI: 10.52420/2071-5943-2022-21-1-77-84.
10. *Перепелица С. А.* Острый респираторный дистресс-синдром у недоношенных новорожденных (морфологическое исследование). *Общая реаниматология.* 2020; 16 (1): 35–44. *Perepelitsa S. A.* Acute respiratory distress syndrome in preterm newborns (morphological study). *General Reanimatology = Obshchaya Reanimatologiya.* 2020; 16 (1): 35–44. (in Russ.&Eng.). DOI: 10.15360/1813-9779-2020-1-35-44.
11. *Голомидов А. В., Григорьев Е. В., Мозес В. Г., Мозес К. Б.* Патогенез, прогнозирование и исходы синдрома полиорганной недостаточности у новорожденных (обзор). *Общая реаниматология.* 2022; 18 (6): 37–49. *Golomidov A. V., Grigoriev E. V., Moses V. G., Moses K. B.* Pathogenesis, prognosis and outcomes of multiple organ failure in newborns (review). *General Reanimatology = Obshchaya Reanimatologiya.* 2022; 18 (6): 37–49. (in Russ.&Eng.). DOI: 10.15360/1813-9779-2022-6-37-49.
12. *Osman A. M., El-Farrash R. A., Mohammed E. H.* Early rescue Neopuff for infants with transient tachypnea of newborn: a randomized controlled trial. *J Matern Fetal Neonatal Med.* 2019; 32 (4): 597–603. DOI 10.1080/14767058.2017.1387531. PMID: 28965435.
13. *Gizzi C., Klifa R., Pattumelli M. G., Massenzi L., Taveira M., Shankar-Aguilera S., De Luca D.* Continuous positive airway pressure and the burden of care for transient tachypnea of the neonate: retrospective cohort study. *Am J Perinatol.* 2015; 32 (10): 939–943. DOI: 10.1055/s-0034-1543988. PMID: 25811328.
14. *Migliori C., Motta M., Angeli A., Chirico G.* Nasal bilevel vs. continuous positive airway pressure in preterm infants. *Pediatr Pulmonol.* 2005; 40 (5): 426–430. DOI: 10.1002/ppul.20276. PMID: 16155882.
15. Реанимация и стабилизация состояния новорожденных детей в родильном зале: методическое письмо Министерства Здравоохранения Российской Федерации от 4 марта 2020 г. № 15–4/И/2–2570 под редакцией профессора Е. Н. Байбариной; 2020: 55. Resuscitation and stabilization of newborns in the delivery room: Methodical instructions of the Ministry of Health of the Russian Federation dated March 4, 2020 No. 15-4/I/2-2570 edited by Professor E. N. Baibarina; 2020: 55. (in Russ.). URL: http: //niiomm.ru/attachments/article/370/Реанимация%20и%20стабилизация%20состояния%20новорожденных%20детей%20в%20родильном%20зале%202020.pdf.
16. Неонатология: национальное руководство: краткое издание. ред. Володин Н. Н. Москва: ГЭОТАР–Медиа; 2019: 896. Neonatology: National guidelines: short edition. ed. Volodin N. N. Moscow: GEOTAR–Media; 2019: 896. (in Russ.). ISBN 978–5–9704–4877–9.
17. *Шестак Е. В., Ковтун О. П., Ксенофонтова О. Л., Додров Д. С., Калякова Н. В.* Респираторные стратегии, влияющие на тяжесть течения транзиторного тахипноэ новорожденных. *Врач.* 2022; (1): 56–60. *Shestak E. V., Kovtun O. P., Ksenofontova O. L., Dodrov D. S., Kalyakova N. V.* Respiratory strategies affecting the severity of transient tachypnea in newborns. *Doctor = Vrach.* 2022; (1): 56–60. (in Russ.). DOI: 10.29296/25877305-2022-01-09.
18. *Шестак Е. В., Ковтун О. П., Ксенофонтова О. Л., Додров Д. С.* Эффективность и безопасность стандартизированного протокола CPAP-терапии доношенных новорожденных в родовом зале при транзиторном тахипноэ: клиническое ис-

следование с историческим контролем. *Вопросы современной педиатрии*. 2022; 21 (4): 320–330. *Shestak E. V., Kovtun O. P., Ksenofontova O. L., Dodrov D. S.* Efficacy and safety of a standardized protocol of CPAP therapy for full-term newborns in delivery room at transient tachypnea: clinical trial with historical control. *Issues of Modern Pediatrics = Voprosy Sovremennoy Pediatrii*. 2022; 21 (4): 320–330. (in Russ.). DOI: 10.15690/vsp.v21i4.2445.

19. *Шестак Е. В., Ковтун О. П.* Стандартизированный подход к CPAP-терапии в родовом зале у доношенных детей с врожденной инфекцией: наблюдательное исследование. *Российский педиатрический журнал*. 2023; 4 (3): 85–93. *Shestak E. V., Kovtun O. P.* Standardized approach to CPAP therapy in the delivery room in full-term infants with congenital infection: observational research. *Russian Pediatric Journal/ Rossiyskiy Pediatricheskiy Zhurnal*. 2023; 4 (3): 85–93. (in Russ.). DOI: 10.15690/rpj.v4i3.2618.
20. *Шестак Е. В., Ковтун О. П.* Прогнозирование тяжести течения транзиторного тахипноэ у доношенных новорожденных в родовом зале. *Российский педиатрический журнал*. 2022; 25 (2): 91–95. *Shestak E. V., Kovtun O. P.* Predicting the severity of the course of transient tachypnea in full-term newborns in the delivery room. *Russian Pediatric Journal/ Rossiyskiy Pediatricheskiy Zhurnal*. 2022; 25 (2): 91–95. (in Russ.). DOI: 10.46563/1560-9561-2022-25-2-91-95.
21. *Мостовой А. В., Карпова А. Л., Володин Н. Н., Петрова А. С., Милева О. И., Захарова Н. И., Дмитриев А. В., с соавт.* Оценка клинической практики проведения респираторной терапии и ее исходов у недоношенных новорожденных гестационного возраста 34–36 недель с респираторным дистресс-синдромом. *Анестезиология и реаниматология*. 2021; (4): 67–72. *Mostovoy A. V., Karpova A. L., Volodin N. N., Petrova A. S., Mileva O. I., Zakharova N. I., Dmitriev A. V., et al.* Evaluation of the clinical practice of respiratory therapy and outcomes in late preterm (34–36 weeks) with respiratory distress syndrome. *Russian Journal of Anesthesiology and Reanimatology/ Anesteziologiya i Reanimatologiya*. 2021; (4): 67–72. (in Russ.). DOI: 10.17116/anaesthesiology202104167.
22. *Kumar A., Bha B.V* Epidemiology of respiratory distress of newborns. *Indian J Pediatr*. 1996; 63 (1): 93–98. DOI: 10.1007/BF02823875. PMID: 10829971.
23. *Ryan C. A. Hughes P.* Neonatal respiratory morbidity and mode of delivery at term: influence of timing of elective caesarean section. *Br J Obstet Gynaecol*. 1995; 102 (10): 843–844. DOI: 10.1111/j.1471-0528.1995.tb10861.x. PMID: 7547751.
24. *Kasap B., Duman N., Ozer E., Tatli M., Kumral A., Ozkan H.* Transient tachypnea of the newborn: predictive factor for prolonged tachypnea. *Pediatr Intl*. 2008; 50 (1): 81–84. DOI: 10.1111/j.1442-200X.2007.02535.x. PMID: 18279211.
25. *Jain L.* Respiratory morbidity in late–preterm infants: prevention is better than cure! *Am J Perinatol*. 2008; 25 (2): 75–78. DOI: 10.1055/s–2007–1022471. PMID: 18214813.
26. *Raju T. N. K., Higgins R.D, Stark A. R., Leveno K. J.* Optimizing care and outcome for late–preterm (near–term) infants: a summary of the workshop sponsored by the National Institute of Child Health and Human Development. *Pediatrics*. 2006; 118 (3): 1207–1214. DOI: 10.1542/peds.2006–0018. PMID: 16951017.
27. *Gomez-Lopez N., Galaz J., Miller D., Farias-Jofre M., Liu Z., Arenas-Hernandez M., Garcia-Flores V., et al.* The immunobiology of preterm labor and birth: intra-amniotic inflammation or breakdown of maternal-fetal homeostasis. *Reproduction*. 2022; 164 (2): R11–R45. DOI: 10.1530/REP-22-0046. PMID: 35559791.
28. *Jiang M., Mishu M. M., Lu D., Yin X.* A case control study of risk factors and neonatal outcomes of preterm birth. *Taiwan J Obstet Gynecol*. 2018; 57 (6): 814–818. DOI: 10.1016/j.tjog.2018.10.008. PMID: 30545533.
29. *Gibbs R. S.* The origins of stillbirth: infectious diseases. *Semin Perinatol*. 2002; 26 (1): 75–78. DOI: 10.1053/sper.2002.29839. PMID: 11876570.
30. *Rawlinson W. D., Hall B., Jones C. A., Jeffery H. E., Arbuckle S. M., Graf N., Howard J., et al.* Viruses and other infections in stillbirth: what is the evidence and what should we be doing? *Pathology*. 2008; 40 (2): 149–160. DOI: 10.1080/00313020701813792. PMID: 18203037.
31. *Goldenberg R. L., Thompson C.* The infectious origins of stillbirth. *Am J Obstet Gynecol*. 2003; 189 (3): 861–873. DOI: 10.1067/s0002-9378 (03)00470-8. PMID: 14526331.
32. *Puopolo K. M., Benitz W. E., Zaoutis T. E.*; Committee on Fetus and Newborn; Committee on Infectious Diseases. Management of neonates born at ⩾ 35 0/7 weeks‘ gestation with suspected or proven early-onset bacterial sepsis. *Pediatrics*. 2018; 142 (6): e20182894. DOI: 10.1542/peds.2018-2894. PMID: 30455342.
33. *Greco P., Nencini G., Piva I., Scioscia M., Volta C. A., Spadaro S., Neri M., et al.* Pathophysiology of hypoxic-ischemic encephalopathy: a review of the past and a view on the future. *Acta Neurol Bel*. 2020; 120 (2): 277–288. DOI: 10.1007/s13760-020-01308-3. PMID: 32112349.
34. *Шестак Е. В., Ковтун О. П., Ксенофонтова О. Л.* Оценка церебральной оксигенации при развитии транзиторного тахипноэ у новорожденных. *Педиатрия. Журнал им. Г. Н. Сперанского*. 2023; 102 (1): 27–35. *Shestak E. V., Kovtun O. P., Ksenofontova O. L.* Assessment of cerebral oxygenation in the development of transient tachypnea in newborns. *Pediatrics. G. N. Speransky J. = Pediatria. Zhournal im. G. N. Speranskogo*. 2023; 102 (1): 27–35. (in Russ.). DOI: 10.24110/0031-403X-2023-102-1-27-35.
35. *Шестак Е. В., Ковтун О. П., Базарный В. В., Полушина Л. Г., Максимова А. Ю.* Диагностическая оценка уровня нейротрофических факторов VEGF, BDNF, β-NGF у новорожденных с транзиторным тахипноэ и церебральной ишемией в сравнении со здоровыми детьми. *Педиатрия. Журнал им. Г. Н. Сперанского*. 2024; 103 (1): 49–57. *Shestak E. V., Kovtun O. P., Bazarny V. V., Polushina L. G., Maksimova A.Yu.* Assessment of the level of neurotrophic factors VEGF, BDNF, β-NGF in newborns with transient tachypnea and cerebral ischemia in comparison with healthy children. *Pediatrics. G.N Speransky J. = Pediatria. Zhournal im. G. N. Speranskogo*. 2024; 103 (1): 49–57. (in Russ.). DOI: 10.24110/0031-403X-2024-103-1-49-57.

Received 11.08.2023
Accepted 10.09 2024