DOI: https://doi.org/10.17816/PED136107-115
Research Article

ENDOBRONCHIAL SURFACTANT ADMINISTRATION IN FULL-TERM NEWBORN WITH RESPIRATORY DISTRESS SYNDROME

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For citation: Ivanov DO, Kiriakov KS, Pshenisnov KV, Tesaeva IA, Nasipova MU, Sizaeva EA, Gabisov AT. Endobronchial surfactant administration in full-term newborn with respiratory distress syndrome. *Pediatrician (St. Petersburg)*. 2022;13(6):107–115. DOI: https://doi.org/10.17816/PED136107-115

Neonatal respiratory distress syndrome is the leading cause of neonatal acute respiratory failure. Despite the successes achieved and the existing international recommendations, in some cases there is a severe course of this disease, which requires a personalized approach to the patient and intensive care measures.

The article presents a case of successful treatment of acute respiratory distress syndrome in a full-term newborn complicated by pulmonary barotrauma using monobronchial administration of exogenous surfactant under X-ray control. In order to assess the course of the disease and the effectiveness of treatment, a retrospective analysis of medical documentation was carried out. From the first minutes of life, the child had respiratory disorders, which was the basis for non-invasive mechanical lung ventilation — nCPAP (nasal continuous positive airway pressure). Progression of hypercapnia and hypoxemia was revealed over time, and therefore tracheal intubation was performed and convective mechanical ventilation was started with FiO_2 = 1,0. Monobronchial administration of exogenous surfactant was a key element of the therapy that allowed to achieve stabilization of the condition and regression of gas exchange disorders with complete recovery of the patient.

Monobronchial administration of surfactant in acute respiratory distress syndrome with heterogeneous lung involvement is an effective treatment option and can be used in clinical practice for refractory hypoxemia.

Keywords: full-term newborn; respiratory distress syndrome; barotrauma; pneumothorax; surfactant.

Received: 11.10.2022 **Revised:** 17.11.2022 **Accepted:** 30.12.2022

DOI: https://doi.org/10.17816/PED136107-115
Научная статья

ЭНДОБРОНХИАЛЬНОЕ ВВЕДЕНИЕ СУРФАКТАНТА У ДОНОШЕННОГО НОВОРОЖДЕННОГО С РЕСПИРАТОРНЫМ ДИСТРЕСС-СИНДРОМОМ (КЛИНИЧЕСКИЙ СЛУЧАЙ)

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Для цитирования: Иванов Д.О., Кирьяков К.С., Пшениснов К.В., Тесаева И.А., Насипова М.У., Сизаева Е.А., Габисов А.Т. Эндобронхиальное введение сурфактанта у доношенного новорожденного с респираторным дистресс-синдромом (клинический случай) // Педиатр. – 2022. – Т. 13. – № 6. – С. 107–115. DOI: https://doi.org/10.17816/PED136107-115

Респираторный дистресс-синдром новорожденных — основная причина острой дыхательной недостаточности в неонатальном периоде. Несмотря на достигнутые успехи и существующие международные рекомендации, в ряде случаев имеет место тяжелое течение данного заболевания, что требует персонифицированного подхода к пациенту и мероприятиям интенсивной терапии.

В статье представлен случай успешного лечения острого респираторного дистресс-синдрома у доношенного новорожденного, осложнившегося баротравмой легких, с применением монобронхиального введения экзогенного сурфактанта под рентгенологическим контролем. С целью оценки течения заболевания и эффективности лечения проведен ретроспективный анализ медицинской документации. С первых минут жизни у ребенка отмечались дыхательные расстройства, что стало основанием для проведения неинвазивной искусственной вентиляции легких. В динамике выявлено прогрессирование гиперкапнии и гипоксемии, в связи с чем была выполнена интубация трахеи и начата конвекциональная искусственная вентиляция легких с FiO_2 = 1,0. Ключевой элемент терапии, позволивший достичь стабилизации состояния и регрессирования нарушений газообмена с полным выздоровлением пациента, — монобронхиальное введение экзогенного сурфактанта.

Монобронхиальное введение сурфактанта при остром респираторном дистресс-синдроме с гетерогенным поражением легких является эффективным вариантом лечения и может использоваться в клинической практике при рефрактерной гипоксемии.

Ключевые слова: доношенный новорожденный; респираторный дистресс-синдром; баротравма; пневмоторакс; сурфактант.

Поступила: 11.10.2022 **Одобрена:** 17.11.2022 **Принята к печати:** 30.12.2022

BACKGROUND

Respiratory distress syndrome (RDS) in newborns is one of the most common and severe critical conditions in the neonatal period [1, 3–5, 7–9, 11]. It has diverse causes and depends primarily on the gestational age of the child upon birth and the morphological and functional maturity of the respiratory organs.

If respiratory failure and acute RDS (ARDS) in premature newborns develop most often in the first hours of life in the presence of primary surfactant deficiency, then in full-term infants, severe hypoxemic respiratory failure is generally secondary and is associated with an already existing pathological process with lesions of the lung parenchyma [1, 5–7]. These are mainly manifested as pneumonia, meconium aspiration syndrome, and transient tachypnea of newborns [5, 7, 10]. RDS developed in approximately 1% of newborns without a respiratory infection. Most often, severe hypoxemia without an infectious component in full-term newborns develops after operative delivery in the presence of transient tachypnea, which can be a precursor of severe ARDS. Although transient tachypnea of newborns has a favorable prognosis and resolves spontaneously within the first 3 days of life, a severe course with refractory hypoxemia occurs in some cases [14]. In particular, pulmonary hypertension, which requires extracorporeal membrane oxygenation, can develop in some children with a gestational age of up to 39 weeks, born by cesarean section [13].

In this study, we present a case of a severe course of transient tachypnea accompanied by secondary ARDS and its successful treatment, which was complicated by pulmonary barotrauma, using monobronchial administration of a surfactant in a full-term newborn.

CLINICAL CASE

A full-term newborn with severe respiratory failure requiring respiratory support was admitted to the Republican Perinatal Center of the Chechen Republic. The birthweight and height were 2400 g and 52 cm, respectively. The 1-min and 5-min Apgar scores were 7 and 8 points, respectively. The child was from the fourth pregnancy and the third term birth at a gestational age of 37.3 weeks by cesarean section. At a gestational age of 15 weeks, the mother contracted a coronavirus infection.

From birth, the child was in a moderately severe state due to respiratory distress (moderate retraction of the intercostal space, grunting breathing, and tachypnea of up to 60 breaths per minute), which required non-invasive artificial lung ventilation (ALV; nasal continuous positive airway pressure [nCPAP]) from the first minutes of life [2]. The radiograph showed signs of transient tachypnea (Fig. 1).

In the course of nCPAP, the progression of respiratory failure was registered. Repeated chest X-ray imaging revealed signs of neonatal RDS; therefore, tracheal intubation was performed, and invasive ALV was started in the SIMV mode with FiO_2 of 0.5, inspiratory pressure (Pinsp) of 16 cm H_2O, positive end-expiratory pressure (PEEP) of 5 cm H_2O, respiratory rate (*f*) of 40 breaths per minute, and inspiratory time (Tinsp) of 0.4 s. Given the presence of arterial hypotension, a volemic load of 15 mL/kg of 0.9% sodium chloride solution was performed, which had no effect, and a constant infusion of dopamine was started at a dose of 5 μg/(kg · min). Until negative markers of inflammation and bacteriological culture were obtained, empirical antibiotic therapy was started [ampicillin at a dose of 200 mg/(kg · day) and gentamicin at a dose of 4 mg/(kg · day)].

Owing to the lack of effect, exogenous surfactant was administered endotracheally at a dose of 200 mg/k; however, the patient's condition continued to worsen, which required an increase in the ALV invasiveness (FiO_2 of 1.0, PIP of 18 cm H_2O, PEEP of 5 cm H_2O, *f* of 40 per minute, and Tinsp of 0.4 s).

The control radiograph, obtained on day 2 of life (after surfactant administration), showed signs of severe RDS complicated by right-sided tension pneumothorax (Fig. 2); therefore, according to emergency indications, drainage of the pleural cavity was performed.

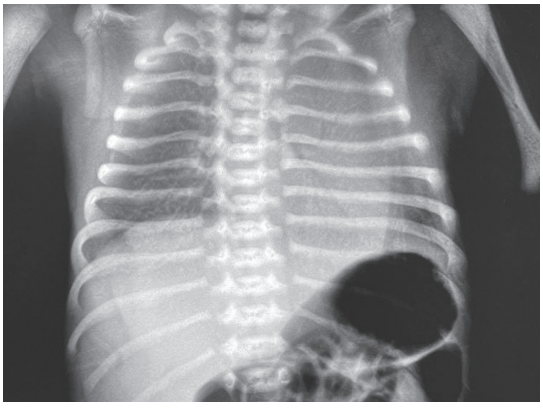

Fig. 1. Chest X-ray of newborn with clinical signs of respiratory distress 2 hours after birth

Рис. 1. Рентгенограмма органов грудной клетки новорожденного с клиническими признаками респираторного дистресс-синдрома через 2 ч после рождения

According to the analysis of the gas composition and acid–base balance (ABB) of venous blood at the time of a sharp deterioration in the condition, decompensated mixed acidosis was noted (pH 7.07, pO_2 27 mm Hg, pCO_2 50 mm Hg, BE18.1 mmol/l, and SvO_2 26%). As the patient had severe arterial hypotension, the dopamine dose was increased to 10 μg/(kg • min).

Over time, episodes of desaturation were noted with a decrease in SpO_2 to 49% at the maximum parameters of ALV; therefore, high-frequency oscillatory (HFO) ALV was started with FiO_2 of 1.0, mean airway pressure (MAP) of 25 cm H_2O, amplitude of 40, frequency of 8 Hz, and inhalation to exhalation ratio of 1:2. Although the dopamine dose was increased to 15 μg/(kg · min), severe arterial hypotension persisted; therefore, adrenaline was added to the therapy at a dose of 0.05 μg/(kg · min), which resulted in the achievement of reference blood pressure indicators.

On the chest radiograph, signs of severe RDS, total opacity of the left lung field, despite active drainage of the right pleural cavity, and parietal right-sided pneumothorax persisted, and air accumulation in the medial section of the right lung was noted.

According to the analysis of the gas composition and ABB of the venous blood, decompensated respiratory acidosis, severe hypoxemia (pvO_2 5 mm Hg), and hyperlactatemia (5.9 mmol/L) were noted. Clinically, there was total cyanosis of the skin, and the SpO_2 30% increased to 7% against HFO ALV with FiO_2 of 1.0, MAP 22 cm H_2O, amplitude of 32, *f* of 8 Hz, and I:E of 1:2.

Against the deterioration of the patient's condition due to multiple organ dysfunction, despite the absence of laboratory signs of a severe infection, antibiotic therapy was corrected; cefoperazone/sulbactam at a dose of 80 mg/(kg · day) and amikacin at a dose of 10 mg/(kg · day) were prescribed.

Given the right-sided pneumothorax and radiographic signs of severe RDS with a predominant lesion of the left lung, a monobronchial poractant alfa was administered. In the course of HFO ALV, poractant alfa at a dose of 100 mg/kg was administered through the endotracheal tube into the left main bronchus. The procedure was performed under X-ray control.

In this context, a pronounced positive effect was noted, i.e., the SpO_2 increased from 7%–23% to 90%. The control radiograph immediately after the administration of poractant alfa (Fig. 3) showed a minor improvement in the left lung pneumatization, and free air remained in the right pleural cavity.

On the control radiograph 6 h after the procedure, signs of right-sided pneumothorax persisted, and uneven restoration of airiness of the left lung was noted. Reducing the HFO ALV parameters was not possible. Subsequently, the respiratory failure progressed with desaturation (SpO_2 46%). The analysis of the gas composition of the venous blood revealed pronounced venous hypoxemia (pO_2 13 mm Hg) and hyperlactatemia (6.7 mmol/L). Severe arterial hypotension persisted; therefore, the rate of adrenaline administration was increased to 0.2 μg/(kg · min), while stabilization was achieved.

Poractant alfa was administered repeatedly to the left main bronchus. After the procedure, a clinical and radiological improvement was noted (Fig. 4), namely, an increase in SpO_2 up to 90% and positive changes in the blood gas composition.

On day 3 of life, 12 h after the repeated administrations of poractant alfa, SpO_2 was 78%–84%, and the skin cyanosis worsened. A repeated radiogram of the chest organs was performed, which revealed the progression of the right-sided pneumothorax and a decrease in the pneumatization of the left lung compared with the image obtained immediately after the administration of poractant alfa. Active drainage of the right pleural cavity was continued. Due to arterial hypotension, the adrenaline dose was increased to 0.3 μg/(kg · min), which induced hemodynamic stabilization, and blood pressure within the age norm. Taking into account the decrease in pneumatization of the left lung and the progression of respiratory failure, a preparation of beractant was administered to the left main bronchus. During the procedure, the SpO_2 decreased to 45%–50%, and skin cyanosis worsened; therefore, the manipulation was stopped. The administration of poractant alfa at a dose of 100 mg/kg into the left main bronchus was started. Subsequently, the patient's condition improved, as evidenced by an increase in SpO_2 up to 98%. An increase in the left lung transparency was registered on the chest radiograph 12 h (Fig. 5) after the surfactant administration.

On day 4 of life (Fig. 6), the control radiograph revealed persisting right-sided parietal pneumothorax and pneumatization of the left lung with improvement. Due to arterial hypotension, constant infusion of dopamine at a dose of 15 μg/(kg · min) was continued, and the adrenaline dose was increased to 0.5 μg/(kg · min).

On day 6 of life, a chest radiograph showed persisting residual effects of a right-sided pneumothorax and an increase in the lung tissue transpar-

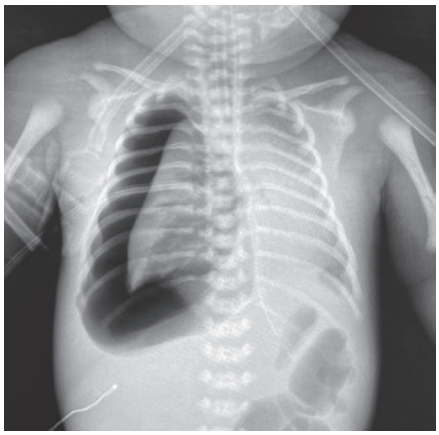

Fig. 2. Chest X-ray of newborn after surfactant administration
Рис. 2. Рентгенограмма органов грудной клетки новорожденного после введения сурфактанта

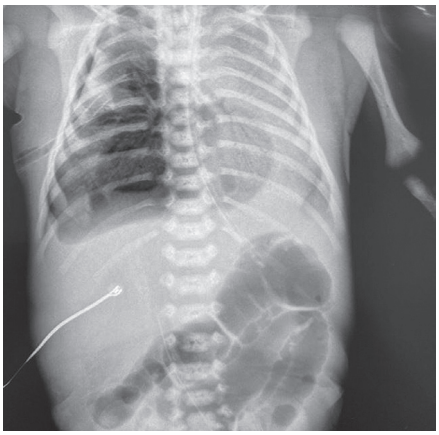

Fig. 3. Chest X-ray of newborn after monobronchial surfactant administration
Рис. 3. Рентгенограмма органов грудной клетки новорожденного после монобронхиального введения сурфактанта

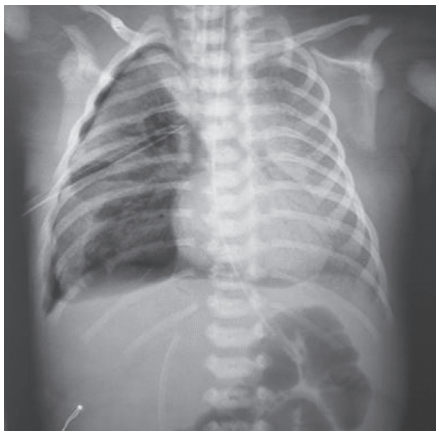

Fig. 4. Chest X-ray of newborn after repeated monobronchial administration of surfactant
Рис. 4. Рентгенограмма органов грудной клетки новорожденного после повторного монобронхиального введения сурфактанта

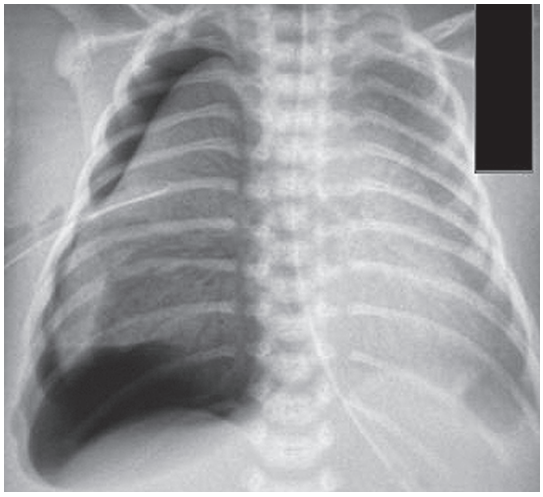

Fig. 5. Chest X-Ray of newborn after monobronchial administration of proractant alpha
Рис. 5. Рентгенограмма органов грудной клетки новорожденного после монобронхиального введения порактанта альфа

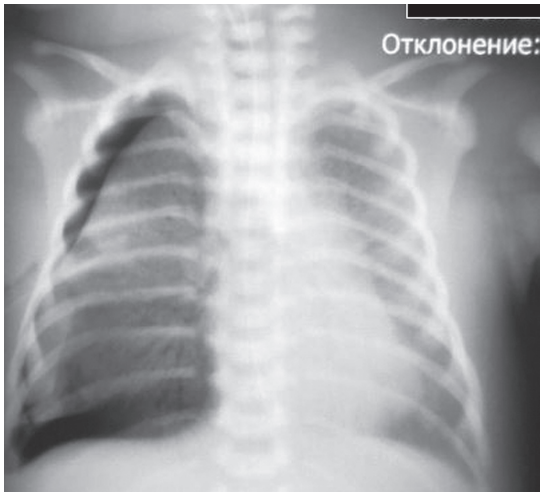

Fig. 6. Chest X-ray of newborn on the sixth day of life
Рис. 6. Рентгенограмма органов грудной клетки новорожденного на шестые сутки жизни

ency on both sides. Heart rate and blood pressure indicators were stable against constant infusions of dopamine at a dose of 15 μg/(kg · min) and adrenaline at a dose of 0.1 μg/(kg · min).

On day 7 of life, respiratory failure progressed, the SpO_2 decreased to 76%, and pulmonary, and gastric bleeding occurred. In connection with arterial hypotension, the adrenaline dose was increased to 0.15 μg/(kg · min). Given the pronounced oxygen dependence in the presence of aggressive respiratory support, an erythrocyte suspension of 15 ml/kg was transfused. The control radiograph showed an increase in focal pneumonia of the right lung, with multiple focal opacities on the left, and free air persisted in the right pleural cavity. Given the deterioration of the clinical presentation, cefoperazone/sulbactam and amikacin were canceled, and meropenem at a dose of 40 mg/kg after 8 h and linezolid at a dose of 10 mg/kg after 8 h were prescribed. Against the stabilization of hemodynamics, the dopamine dose was reduced to 3 μg/(kg · min) and that of adrenaline to 0.1 μg/(kg · min).

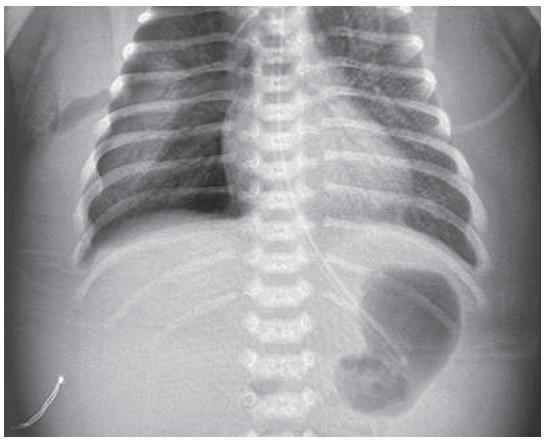

Fig. 7. Chest X-ray of newborn on the ninth day of life
Рис. 7. Рентгенограмма органов грудной клетки новорожденного на девятые сутки жизни

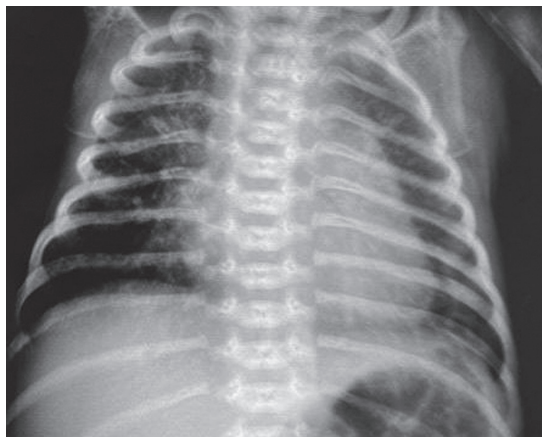

Fig. 8. Chest X-ray of newborn with spontaneous breathing
Рис. 8. Рентгенограмма органов грудной клетки новорожденного на фоне спонтанного дыхания

On day 9 of life, the patient's condition was stable, the gas composition, and ABB of venous blood were compensated, the ALV parameters were reduced, and the pleural drainage was removed (Fig. 7).

Given the gradual decrease in ALV parameters, the patient was switched from HFO to convection ALV (FiO_2 of 0.45, Pinsp of 12 cm H_2O, PEEP of 5 cm H_2O, O, *f* of 35 per minute, and Tinsp of 0.4 s). Hemodynamics was stable without inotropic support, and the blood pressure was within the age norm. The radiograph showed multiple focal opacities in the lungs, predominantly on the right.

Given the stable condition of the patient and the absence of signs of a progressive infectious and inflammatory process according to laboratory data, antibiotic therapy was continued in the same volume. To improve mucociliary clearance, acetylcysteine was added to the therapy at a dose of 10 mg/kg after 12 h.

On day 12 of life, the child had regular spontaneous breathing, restoration of protective reflexes, and muscle tone; thus, the child was extubated, and switched to non-invasive ALV with FiO_2 of 0.3, PEEP of 5 cm H_2O, and *f* of 7.0 per min. No pronounced pathological changes were noted in the control radiograph of the chest organs (Fig. 8).

By day 26 of life, respiratory support was canceled, the patient had no oxygen dependence, and the SpO_2 values were within the reference values. On day 33 of life, the child was transferred to the neonatal pathology department in a satisfactory condition for further treatment. The table presents the dynamics of blood gas composition and lactate concentration in the blood serum against the therapeutic measures.

The durations of invasive lung ventilation, non-invasive ALV after extubation, and treatment in the intensive care unit were 360 h, 192 h, and 27 days, respectively. The child was discharged from the hospital on day 31 of life with the primary diagnosis of transient tachypnea of newborns, ARDS, and pneumonia of the newborn. The patient had no complications in the respiratory and central nervous systems.

DISCUSSION

A distinctive characteristic of this case is the extremely severe course of ARDS in a full-term newborn, which developed in the presence of respiratory metabolism disorders caused by transient tachypnea of newborns. Despite the timely non-invasive respiratory support, which was used from the first minutes of life, severe respiratory disorders progressed, which required tracheal intubation, and transfer to convection ALV and then to HFO ALV with aggressive parameters, which was one of the factors that aggravated the severity of the patient's condition that provoked the development of air leak syndrome and multiple organ dysfunction syndrome [3, 12].

Thus, the staging course of the disease must be emphasized. Initially, the severity of the child's condition was due to transient tachypnea of newborns, and further progression of hypoxemia led to secondary lung damage and ARDS development. In later disease stages, most probably, postnatal infection occurred, which caused the emergence of clinical and radiological signs of pneumonia. distinctive characteristic of this case is the presence of persistent hypoxemia with relatively acceptable levels of carbon dioxide tension in the blood, which

Table / Таблица

Parameters of gas composition and lactate concentration in venous blood of newborn
Показатели газового состава и концентрации лактата в венозной крови новорожденного

Age of child / Возраст ребенка	pH	pO_2, mm Hg / мм рт. ст.	pCO_2, mm Hg / мм рт. ст.	Lactate, mmol/l / Лактат, ммоль/л
2 hours 12 minutes / 2 ч 12 мин	7.2	37	57	4.2
9 hours (after administration of the beractant) / 9 ч (после введения берактанта)	7.28	43	35	3.1
27 hours 30 minutes (tension pneumothorax) / 27 ч 30 мин (напряженный пневмоторакс)	7.07	27	50	5.6
28 hours 50 minutes (after drainage of the pleural cavity) / 28 ч 50 мин (после дренирования плевральной полости)	7.43	36	38	7.4
41 hour 30 minutes / 41 ч 30 мин	7.16	5	87	5.9
44 hours 30 minutes / 44 ч 30 мин	7.29	23	51	6.6
46 hours 50 minutes (after administration of poractant alpha) / 46 ч 50 мин (после введения порактанта альфа)	7.27	23	48	6.0
49 hours 25 minutes / 49 ч 25 мин	7.33	13	44	6.7
53 hours / 53 ч	7.4	35	40	4.2
58 hours 20 minutes / 58 ч 20 мин	7.4	45	35	4.0

indicated the presence of secondary pulmonary hypertension in the child, especially considering that at the time of birth, his gestational age was 37.3 weeks.

Given the heterogeneity of lung tissue lesions with a predominant lesion in one lung, the course of the infectious process was suspected. Under X-ray control, an exogenous surfactant was administered into the left main bronchus, and the patient's condition stabilized for a short time. Subsequently, the severe hypoxemic respiratory failure progressed, and only repeated monobronchial injections of exogenous surfactant helped achieve a stable positive therapeutic effect and contributed to the regression of a critical condition with a high risk of lethal outcome.

CONCLUSION

Monobronchial administration of exogenous surfactant in secondary ARDS with heterogeneous lung lesions is an effective treatment option and can be used in clinical practice for refractory hypoxemia as a salvage strategy.

ADDITIONAL INFORMATION

Author contribution. Thereby, all authors made a substantial contribution to the conception of the study, acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study.

Competing interests. The authors declare that they have no competing interests.

Funding source. This study was not supported by any external sources of funding.

Consent for publication. Written consent was obtained from the patient for publication of relevant medical information and all of accompanying images within the manuscript.

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