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Effective Ventilation Mode in Early Neonatal Sepsis, Bilateral Pneumonia, and Pulmonary Hypertension in a Very Low Birth Weight Newborn (Case Report)

Konstantin V. Lukashev[1,2], Alexander I. Nuzhdin[3], Alexey.T. Emikh[1]*, Anna N. Grishina[1], Elena B. Zorina[1], Nikolay V. Shleikher[1], Sergey L. Kan[2], Yulia V. Kovaleva[1]

[1] G. P. Kurbatov City Clinical Hospital No. 1,
28 Prospect Bardina, 654057 Novokuznetsk, Russia
[2] Novokuznetsk State Institute for Physicians Advanced Training,
Branch of the Russian Medical Academy for Continuous Professional Education, Ministry of Health of Russia,
5 Stroiteley Av., 654005 Novokuznetsk, Kemerovo Region, Russia
[3] Maternity Hospital No. 7 for Novosibirsk Region
4 Geroev Revolyutsii Str., 630037 Novosibirsk, Russia

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***Correspondence to:** Alexey T. Emikh, aleksei7493@mail.ru

Summary

The aim was to demonstrate an alternative approach to respiratory therapy in respiratory failure complicated by pulmonary hypertension when conventional ventilation and high-frequency oscillatory ventilation are ineffective.

Patient and study methods. We analyzed laboratory data, ventilatory parameters and hemodynamic parameters during ventilation in a child with birth weight of 1300 grams and respiratory failure complicated by pulmonary hypertension. Dynamic selection of parameters and modes of pulmonary ventilation with transition to Airway Pressure Release Ventilation (APRV) mode is presented. Chest radiography and echocardiography were used.

Results. The use of APRV mode when traditional approaches were ineffective allowed «stabilization» of the lungs by alveolar recruitment without deep sedation and muscle relaxation. On day 20 after birth, the infant was weaned. On day 29, the infant was transferred to the neonatal pathology unit for further management, and on day 49, the infant was discharged in stable condition.

Conclusion. In neonates with severe respiratory failure, the use of the APRV mode as an alternative to ineffective conventional ventilation requires further investigation and the development of guidelines for its use.

Keywords: Bi-Vent; APRV; high-frequency oscillatory ventilation; neonatal pneumonia; early neonatal sepsis; neonatal pulmonary hypertension; low birth weight neonate; neonatal distress syndrome

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

Introduction

Congenital pneumonia is an acute infectious disease with predominant lower respiratory tract damage and accumulation of inflammatory exudate inside the alveoli, detected by physical and radiologic examination, usually within the first 72 hours after birth [1]. Congenital pneumonia may be complicated by neonatal sepsis, which clinically manifests as a systemic infection in the first 28 days of life. It is usually classified as early (<48–72 h) or late (>48–72 h) sepsis, depending on the child age on onset [2].

A recent meta-analysis by Fleischmann S. et al. reported an incidence of neonatal sepsis of 2,824 cases per 100,000 live births for the period January 1979 to May 2019 [3].

The European guidelines for the treatment of neonatal respiratory distress syndrome (NRDS) published in 2022 recommend non-invasive ventilation combined with surfactant administration for premature infants with respiratory distress and, if indicated, subsequent transition to lung ventilation (LV) or high-frequency oscillatory ventilation (HFOV) if non-invasive ventilation is ineffective [4]. However, the Russian NRDS guidelines recommend non-invasive ventilation combined with surfactant administration and when indicated transition to lung ventilation and followed by, if ineffective, transition to HFOV [5].

Thus, both European and Russian guidelines for NRDS do not provide alternative ventilation options when traditional methods are ineffective.

One ventilation option in the treatment of adult respiratory syndrome in the clinical guidelines of the Russian Federation of Anesthesiologists and Reanimatologists is airway pressure release ventilation (APRV) [6, 7]. APRV is proposed as a method to improve gas exchange in severe RDS and was first described in 1987 by M. Stock et al. [8]. Opinions on the effectiveness of the APRV mode are mixed due to limited data on its use and unclear criteria for selecting mode settings [9–11]. In 2019, the first systematic review on the use of this mode in adults was published; however, the authors themselves acknowledge the

challenge of interpreting clinical data due to the lack of clear approaches [12]. In 2023, Shreyas A. et al. published a study comparing APRV and HFOV in 90 infants and concluded that APRV is an effective rescue method of lung ventilation. The study showed comparable survival rates for infants ventilated with either APRV or HFOV mode, with APRV mode achieving similar ventilation and oxygenation goals. However, the need for further studies was confirmed [13].

The possibility of spontaneous breathing by the patient in any phase of the respiratory cycle in this ventilation mode is similar to the «Bi-Vent» mode with two pressure levels, where the lower pressure level (PEEP) and the upper pressure level (P_{high}) are set [14, 15]. The difference between the APRV mode and the Bi-Vent mode is the inverted inhalation/exhalation (I:E) ratio, which promotes alveolar recruitment, opening, and stabilization of the volume of the recruited alveoli [16, 17].

The aim of our work was to demonstrate an alternative approach to respiratory therapy in respiratory failure complicated by pulmonary hypertension with ineffective conventional and HFO ventilation.

In this clinical situation, we encountered respiratory failure in a child complicated by pulmonary hypertension, resistant to conventional and HFOV, requiring the search for alternative ventilation options to stabilize his condition. APRV (Airway Pressure Release Ventilation) was chosen as a «last resort» therapy because this mode of ventilation reduces the risk of barotrauma due to optimized PIP control and does not require deep sedation and the use of muscle relaxants.

Medical History

The child was from the first pregnancy, the mother was regularly examined in the antenatal clinic from the 7th week of pregnancy. In the first half of the pregnancy, marginal placenta previa was noted. In the second half of the pregnancy, edema, hypertension, and proteinuria were observed from the 27th week of gestation, and prenatal fetal lung stimulation was done at the 28th week of gestation. Magnesium administration and antihypertensive therapy (methyldopa 2,000 mg/day, nifedipine 10 mg three times a day) were started at 28 weeks' gestation.

At 31 weeks' gestation, the patient was admitted to the perinatal center with elevated blood pressure (BP) up to 170/100 mmHg, progressive edema of the lower extremities, and decreased urine output during the previous 3 days. Delivery was performed by cesarean section due to severe pre-eclampsia and lack of conditions for natural delivery.

Diagnosis during labor: Premature operative labor at 31 weeks and 5 days gestation. Complication: Severe pre-eclampsia with underlying chronic hypertension. Fetal growth retardation, grade I. Breech presentation of the fetus. Associated: Obesity, 1st degree; myopia, 1st degree; urolithiasis. Surgery: Emergency cesarean section.

Clinical Case and Discussion

The child was born by cesarean section with a body weight of 1,300 grams, Apgar score of 5/6/6 points, Silverman score of 4–5 points, mask ventilation was performed in the delivery room with transition to CPAP, after which the child was transported to the neonatal intensive care unit (NICU).

Clinical diagnosis of the infant. Very low birth weight (1,300 grams). Early neonatal sepsis (severe condition, multiorgan failure syndrome, onset in the first 72 hours after birth). Neonatal infection of undetermined etiology. Congenital bilateral pneumonia (radiologic findings, severe respiratory failure, onset in the first 72 hours of life).

Associated: Respiratory distress syndrome (based on radiologic findings, need for respiratory support and administration of surfactant). Pulmonary hypertension (pulmonary artery pressure 50 mmHg).

Complication: Multiple organ failure syndrome (cardiovascular + respiratory + intestinal), nSOFA score 11 points.

Background: Prematurity 31 weeks.

Risk factors for neonatal infection included very low birth weight, prematurity, and cesarean delivery [18].

On admission to the NICU, we continued respiratory support in the mode of non-invasive lung ventilation (NIV) with pressure control through DragerBabyFlowProng size «L» nasal cannulas (MaquetServoI device). Ventilation parameters are listed in Table 1. Taking into account the gestational age of the infant, the need for NIV respiratory therapy, Silverman score > 3 points in the first 3–6 hours of life, and the need for FiO_2 up to 0.4, surfactant was administered endotracheally by INSURE, after which the oxygen fraction (FiO_2) was reduced to 0.25. NIV was continued in the previous mode.

Antibiotic therapy was administered according to the «starting» protocol (ampicillin + amikacin). Clinical deterioration was observed within 8 hours. Despite NIV, respiratory insufficiency increased, tachypnea up to 90/min and SpO_2 80–82% were recorded. With persistent respiratory distress syndrome (RDS) according to the radiological data, tachypnea on ventilatory support, SpO_2 decrease, the child was transferred to lung ventilation: tracheal intubation was performed with ETT 3.0 mm to a depth of 7 cm from the upper lip, and ventilation was started in intermittent mode with pressure control (MaquetServoI) (Table 1).

On the 2nd day after birth there were episodes of desaturation up to 80%, ultrasound screening of the lungs showed signs of right-sided non-tension pneumothorax, we started therapy according to the protocol

Table 1. Mechanical ventilation modes during the observation period.

Ventilation mode	Lung ventilation settings								
	F, inspirations/s	PEEP, cm H_2O	PIP, cm H_2O	I:E, inspiration/expiration ratio	T_{ins}, s	T_{ins}, %	MAP, cm H_2O	FiO_2	SpO_2, %
Day 1									
nSIMV	30 (60)	5	15	1:2	0.60	20	8	0.4	99
nSIMV	30 (60)	5	15	1:2	0.60	20	8	0.25	82
SIMV	30 (60)	5	18	1:2	0.33	5	10	0.25	99
Day 1									
SIMV	30 (60)	5	18	1:2	0.33	5	10	0.25	80
PC	60 (60)	4	21	1:2	0.33	5	12	1.0	99
Day 3, before 5:30 p.m.									
PC	60 (60)	6	26	1:2	0.33	5	14	1.0	65
PC	60 (60)	7	30	1:2	0.33	5	16	1.0	75
PC	60 (60)	8	35	1:2	0.33	5	20	1.0	70
Day 3, after 5:30 p.m.									
HFOV	P_{mean} 20–22 cm H_2O, △P 35 cm H_2O, Respiratory rate 12–15/min							1.0	70–78
Day 3, from 8:30 p.m.									
APRV / BiVent	P_{high} 35–30 cm H_2O, PEEP 3 cm H_2O (auto PEEP 9 cm H_2O), TP high 0.45 s, PS more than P_{high} 14 cm H_2O, T_{PEEP} 0.15 s, PS higher than PEEP 24 cm H_2O, RR 100 per minute, I:E 3:1, Inspiratory rise time 0.15 s, $V_{t\,ins}$ 20 mL, $V_{t\,exp}$ 25 mL, $V_{t\,exp}$ 3.1 L/min						25–20	1.0	90–95
Day 14									
PC	50 (60)	6	18	1:2	0.40	5	11	0.3	99

of air leak syndrome with FiO_2 100%. Ventilation was performed in pressure control mode (Table 1).

Chest x-ray (Fig. *a*) and echocardiography (Table 2) were performed.

On day 3 after birth, at 15:30, a dramatic negative change in the child's status was observed. Chest x-ray (Fig. *b*) and echocardiography (Table 2) were performed again.

Thus, the pre-existing respiratory failure of parenchymal type was complicated by pulmonary hypertension. It was treated according to current clinical guidelines [19]. Levosimendan was administered as a loading dose of 12 μg/kg followed by a maintenance dose of 0.1 μg/kg/min in combination with sildenafil 1.5 mg/kg twice daily. Cardiotonic support with dobutamine was started at 2 μg/kg/min and gradually increased to 10 μg/kg/min. Vasopressor support with epinephrine was also provided, starting at 0.1 μg/kg/min and gradually increasing to 0.7 μg/kg/min to maintain cardiac output and mean arterial pressure, taking into account «rigid» ventilatory parameters. Nitric oxide was not used.

Low SpO_2 parameters (65–75%) persisted during pressure-controlled ventilation (Table 1).

Taking into account the severity of the disease, increasing deterioration, high risk of death, multiorgan failure syndrome, ongoing neonatal infection, persistent low blood oxygenation, antibiotic therapy was revised, «reserve» antibiotics (meropenem + vancomycin) were prescribed, and non-specific immunoglobulin was added to the treatment.

At 17.30, taking into account the failure of ventilation in pressure control mode with «rigid» parameters, the need for high PIP up to 35 cm H_2O, MAP up to 20 cm H_2O, FiO_2 of 1.0, the patient was transferred to HFOV (Table 1). After that, SpO_2 increased slightly (up to 70–78%). A chest x-ray was performed (Fig. *c*).

In view of transfer to HFOV, sedation was started with fentanyl 0.005% in an age-appropriate dosage. Blood acid-base balance (ABB) showed compensated metabolic acidosis and normocapnia (Table 3). ABB was monitored in capillary blood.

At 20:30, due to the ineffectiveness of HFOV, negative radiological changes, low blood oxygenation (SpO_2 70–78%), high risk of barotrauma, and high probability of death, BiVent/APRV mode was used as an alternative method of ventilation (Table 1). A distal flow sensor was placed in the ventilation circuit. Normalization of SpO_2 to 90–95% was observed within a few minutes. Chest radiography was performed (Fig. *d*).

This mode of ventilation was chosen because of available literature data on its use in pediatric and adult practice [9, 20–24].

After stabilization of the child's condition, the previous therapy was continued.

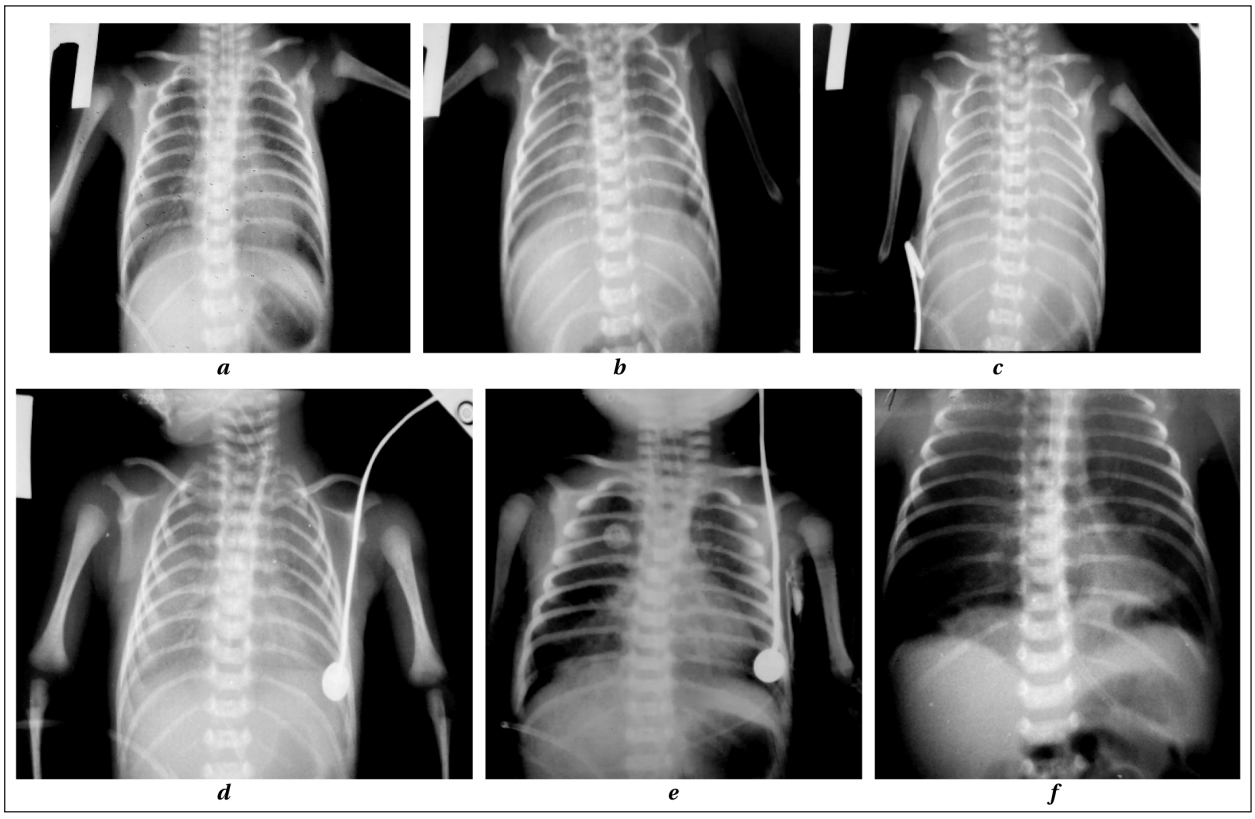

Fig. Chest radiography during the study stages.
a — PC mode ventilation (day 2); *b* — PC mode ventilation (day 3); *c* — HFOV (day 3); *d* — 3 h after switching to APRV mode; *e* — 22 h after switching to APRV mode; *f* — PC mode ventilation (day 14).

Table 2. Change of echocardiographic parameters during study stages.

Parameter	Values		
	Day 2	Day 3	Day 4
Right ventricle diameter, cm	0.7	1	0.6
Interventricular septum, cm	0.28	0.22	0.25
Left ventricular end diastolic diameter, cm	1.2	1.1	1.1
Left ventricular end systolic diameter, cm	0.7	0.6	0.7
Left ventricular posterior wall, cm	0.21	0.2	0.2
Ejection fraction, %	>65	>65	>65
Pulmonary artery pressure, mm Hg	<30	=50	=34

On day 4, echocardiography (Table 2) and chest radiography were performed (Fig. *e*).

In this case, the APRV ventilation mode allowed the setting of a sufficient PIP level corresponding to *P*-high, which was at the same time much lower than in «assisted» and pressure-controlled «classical» ventilation, but allowed to maintain a high MAP, and the inspiratory inversion allowed to prolong the inspiratory phase in the respiratory cycle at a stable frequency, which promoted alveolar recruitment without changing the respiratory volume, which further allowed to smoothly reduce PIP (*P*-high) and MAP with subsequent reduction of gas flow and the risk of barotrauma. High AutoPEEP (due to prolonged inspiratory and expiratory phases and inversion of the I:E ratio) helped to increase functional residual capacity (FRC). Such a long period of APRV mode use was based on the results of acid-base balance and chest x-ray.

Further improvement of the patient's condition was observed with normalization of glycemia, lactate and procalcitonin levels (Tables 3, 4). The evolution of the complete blood count values is shown in Table 5.

A chest x-ray was performed (Fig. *f*).

Metabolic acidosis was corrected with 4% sodium bicarbonate and 2 mL/kg cytoflavin in 5% glucose solution in a 1/5 ratio (this combination was chosen to prevent hypernatremia and encephalopathy) [25]. Respiratory alkalosis was corrected by gradually decreasing P-high and adjusting the I:E ratio with a «shift» from reversible APRV mode to Bi-vent mode (E:I 3:1; 2:1; 1:1; 1:1; 1:2) and further transition to conventional ventilation under blood ABB control (Table 3).

On postnatal day 14, the mode of ventilation was changed from endotracheal tube to pressure-controlled support (Table 1).

Table 3. Changes in blood ABB.

Time of measurement	Values						
	pH	pCO_2, mm Hg	pO_2, mm Hg	BE(B), mmol/L	HCO_3(std), mmol/L	Glucose, mmol/L	Lactate, mmol/L
Day 1							
14:59	7.35	34	44	–5.5	20.2	5.3	4.8
21:05	7.29	43	42	–5.5	19.4	8.3	3.2
21:42	7.34	35	48	–6.1	19.9	5.6	3.1
Day 2							
05:36	7.39	31	42	–4.8	20.7	4.5	3.9
15:33	7.38	26	32	–7.7	18.3	7.9	4.9
Day 3							
13:23	7.32	34	41	–7.4	17.6	5.0	2.4
15:33	7.30	36	35	–7.8	17.7	5.8	3.5
17:30	7.30	41	20	–5.6	20.7	6.9	2.9
19:05	7.38	41	24	–1.1	24.3	8.6	2.6
20:55	7.24	39	31	–10.1	16.3	13.0	8.0
23:05	7.28	32	30	–10.6	15.2	14.5	12.3
02:16	7.26	38	29	–9.0	17.5	17.1	14.9
05:26	7.37	38	35	–3.1	22.0	13.1	12.6
Day 4							
13:11	7.53	42	112	11	33.5	10.3	4.5
19:43	7.65	35	109	16.6	37.8	6.2	3.4
1:51	7.57	38	93	11.7	34.0	5.0	2.4
Day 8							
13:00	7.46	24	48	–5.1	20.8	3.8	1.8
Day 13							
13:00	7.43	25	72	–6.2	20.0	4.7	1.5

Table 4. Changes in inflammatory markers.

Day in NICU	Values	
	Procalcitonin, ng/mL	C-reactive protein, mg/L
1	—	0
4	>10	24
8	0.5–2.0	7
17	0	5

Note. Procalcitonin was measured by immunochromatographic analysis.

Table 5. Changes in CBC

Parameter	Values on days of study				
	1	2	4	8	14
WBC, 1×10^9/L	14.4	24.3	24.6	25.9	17.3
RBC, 10×10^{12}/L	4.29	4.73	3.71	2.94	5.16
HGB, g/L	179	194	150	112	154
HCT, %	51.2	55.1	42.0	32.2	45.7
PLT, 10×10^{12}/L	256	270	185	220	378
WBC differential, %					
Eosinophils	2	2	2	1	1
Bands	7	7	9	8	7
Segments	39	51	46	61	58
Lymphocytes	41	30	30	22	22
Monocytes	11	10	13	8	12

On postnatal day 20, the infant was weaned from the ventilator, and on postnatal day 29, the infant was transferred to the neonatal pathology unit for further management.

After reaching 49 days after birth, the infant was discharged in stable condition at 38 weeks postconceptional age.

Conclusion

When traditional ventilation approaches proved ineffective in a neonate with very low birth weight, early neonatal sepsis, bilateral pneumonia, pulmonary hypertension, and severe respiratory failure, the use of the airway pressure release ventilation (APRV) mode allowed «stabilization» of the lungs by alveolar recruitment. Adaptation of the ventilated infant and stabilization of central hemodynamics and pulmonary blood flow were achieved without the use of «harsh» and dangerous methods such as deep sedation and administration of muscle relaxants. Further research into the APRV mode as an alternative to ineffective conventional ventilation is needed, as well as the development of recommendations for its use.

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